BRIDGED BICYCLIC COMPOUNDS

THESIS

presented to the University of Glasgow

for the degree of Ph.D.

by

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1970

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SUMMARY

This thesis is concerned with the synthesis, spectral properties and reactivities of bicyclo(5.3.1.)undec-7ene-11-one and bicyclo(5.3.1.)undec-7(11)-ene-8-one in each of which the double bond is at the bridgehead, in defiance of Bredt's rule. These compounds were prepared by stereo-specific β-elimination of bicyclic intermediates synthesised by elaboration of cyclooctanone. The spectroscopic properties of the two enones have been compared and the structure and geometry of the former has been determined by X-ray analysis of a heavy atom derivative. The main deformations found were an 8° twist in the π bond of the alkene and a 38° departure from coplanarity in the enone as a whole. This latter value compares favourably with the value of 41.5° obtained by calculation from the ultra-violet spectrum using an empirical relationship.

I wish to express my sincere appreciation and gratitude to Professor R.A Raphel and to Dr G.L Buchanan for the opportunity to carry out this research and to the latter for his unfailing encouragement and advice during the past three years.

I should also like to thank the following for technical services :

Infra-red	Mrs F Lawrie and Mrs N Macniven
Microanalysis	Mr J.M.L Cameron B.Sc., and his Staff
N.M.R	Mrs S.J Humphries and Mrs M.M Kirkland
Mass spectra	Mr A Ritchie
G.L.C	Mr A.D Wylie and Miss I Ninian
Large scale preparation	Mr I McCron

The work described in this Thesis was performed during the tenure of a Maintenance Award from the United States Air Force European Office of Aerospace Research and to this body I express my sincere gratitude.

SUMMARY

This thesis is concerned with the synthesis, spectral properties and reactivities of bicyclo(5.3.1.)undec-7ene-11-one and bicyclo(5.3.1.)undec-7(11)-ene-8-one, in each of which the double bond is at the bridgehead, in defiance of Bredt's rule. These compounds were prepared by stereospecific β-elimination of bicyclic intermediates synthesised by elaboration of cyclooctanone. The spectroscopic properties of the two enones have been compared and the structure and geometry of the former has been determined by X-ray analysis of a heavy atom derivative. The main deformations found were an 8° twist in the π bond of the alkene and a 38° departure from coplanarity in the enone as a whole. This latter value compares favourably with the value of 41.5° obtained by calculation from the ultra-violet spectrum using an empirical relationship.

CONTENTS

I N T R O D U C T I O N

During the period 1902 - 1920 Bredt found that many derivatives of the Camphane and Pinane series showed unexpectedly high resistance to double bond formation. This lack of reactivity is exemplified by the failure of (1) to dehydrochlorinate[1]; of (2) to dehydrobrominate[2] and of (3) to decarboxylate[3]. This resistance to alkene formation is elegantly illustrated by Bredt's work[4] on α-bromocamphoric acid anhydride (4). Even under forcing conditions this bromoanhydride could not be made to dehydrobrominate, nor could the compound (5) be obtained by the circuitous route outlined in Scheme 1, the isomer (5A) being obtained instead.

This illustration of the reluctance of small, bridged, bicyclic systems to tolerate a double bond having one terminus at the bridgehead, together with other cases observed in similar systems, led Bredt to say[5], in 1924 "On the basis of our conception of the position of atoms in space, in camphane and pinene systems, as well as in similarly constituted compounds, a carbon double bond cannot occur at the bridgehead". Bredt advanced this statement, which has come to be known as Bredt's rule, as a qualitative generalisation describing structural limitations in bridged bicyclic systems. However, in 1927, he conceded[6] that, if the rings were sufficiently large, a double bond would be

tolerated at the bridgehead.

Confirmation of this prediction was obtained by the classic work[7] of Prelog, (Scheme 2), in which he set out to define the limits of Bredt's rule. He studied the cyclisation of the diketoester (6) using a refluxing mixture of glacial acetic and concentrated hydrochloric acids, and of the vinyl chloride (7), with concentrated sulphuric acid. The former yielded conjugated enones (8) and/or (9), whilst the latter yielded non-conjugated (10) and/or conjugated (11) bicyclic enones. In each case, the smallest isolated, bridged, bicyclic enone which included an anti-Bredt double bond was the bicyclo (5, 3, 1) undecene system, and Prelog therefore concluded that this represented the boundary of Bredt's rule.

However, the reaction conditions used by Prelog were such that the products were under thermodynamic control. In fact, two separate equilibria are involved. There is some evidence[8] that <u>bridged</u> bicyclic products are formed faster than <u>fused</u> bicyclic products and in consequence, the acetic/hydrochloric acid method of cyclisation gives rise to bridged <u>and</u> fused bicyclic ketones, whereas the concentrated sulphuric acid method yields only bridged products. In other words, in the cyclisation of (6) there is no means of removing the water produced by dehydration of the intermediate aldols, and since all of the reaction

steps leading to (8) and (9) are reversible, an equilibrium is achieved and the product ratio reflects the relative thermodynamic stabilities of the two isolated products. The cyclisation of (7) however, is achieved under conditions where the water eliminated by aldol dehydration is no longer available for the reverse step, i.e under conditions of kinetic control. Nevertheless, the reaction conditions still allow the double bond to equilibrate between the α-β and β-γ positions and again the product ratio reflects the relative stabilities of the two products. These factors account for the observed differences in product distribution between the two cyclisations, despite the fact that both have been shown[9] to proceed via the same intermediate (6).

Thus Prelog confirmed that bridgehead alkenes could be synthesised if the rings were sufficiently large to accommodate the strain. The results obtained in these investigations are however, significant only in the particular case chosen for study, since strain factors are partially counterbalanced by substituent and conjugative effects. Thus the bridgehead alkene moiety in (10) is stabilised by the carbonyl function at C-11 and by being in a tetrasubstituted environment at the bridgehead, as opposed to the trisubstituted position it would be obliged to occupy as the isomeric enone (11).

In the early 1950's these facts were overlooked and it seemed that there was little more to be done in this field. The subject was reviewed[10] by Fawcett, who introduced the concept of an 'S' number for such compounds. (In a bicyclo (x, y,z) system S = x + y + z provided neither x, y nor z equal zero). Prelog's work had demonstrated the ability of a bicyclo 5, 3, 1 system (S = 9) to tolerate a $\Delta^{7,8}$ bridgehead olefin and Fawcett placed the tentative lower limit of ring size for isolable compounds at S = 8 and for transient intermediates at S = 6. There were no valid exceptions to this. Thus a bicyclo (4, 4, 1) undec-1-ene described by Dauben[11] has still an S number of 9. The decarboxylation of the azabicyclononane (12) which appeared to contravene Fawcett's definition, was shown[12] to proceed via (13) by a retro-Mannich reaction followed by recyclisation to (14).

The concept of an 'S' number, however, was not wholly satisfactory as Fawcett pointed out[10]. It failed to distinguish between varying degrees of strain associated with bridgehead olefins contained in the various branches of a bicyclic system. This is illustrated by the fact that the keto-acid (15) does not incorporate deuterium at all[13], whereas ketone (16) readily incorporates 3 atoms of deuterium[14]. Although both systems are of the bicyclo (3, 3, 1) nonane skeleton (S = 7), the former requires a

1 branch enol, whereas the latter requires a 3 branch enol.

This lack of distinction was also apparent in the study of the decarboxylation of β-keto-acids, e.g the β-keto-acid (17) is readily decarboxylated at 145°C[15], whereas the isomer (15) does not lose carbon dioxide at 250°C.[13]. This may be due to greater strain involved in a double bond in a 1 branch than in a 3 branch or, perhaps, for a reason which has little relation to the stability of bridgehead alkenes.[15]

It was now apparent that both Prelog and Fawcett had oversimplified the situation. It was at this point that we entered the field and very significant advances have been made since then.

The first constructive revision has come from Wiseman[16], who considered the general case (18) and noted that the double bond must be trans either in ring "ac" or in ring "ab". On the hypothesis that the strain in a bridgehead olefin is related to the strain in trans-cycloalkenes, he has suggested that since the smallest isolable trans-cycloalkene is trans-cyclooctene, the smallest bridgehead alkenes isolable will be those contained in a bridged bicyclic system in such a way that the double bond is trans in an eight-membered ring. This postulate, which was apparently foreshadowed by Robinson[17] some 17 years ago, has recently been put to the test and

several bridgehead olefins (19)[16,18], (20)[19] and (21)[20] have been synthesised containing transcyclooctene moieties. Wiseman has recently produced evidence[21] of trans-cycloheptenes contained in a bridged bicyclic system, but although he expected such compounds to be more stable than transcycloheptene itself, the products were not isolateable.

The postulate is further borne out by calorimetry studies[22], which show that the strain in bicyclo (3, 3, 1) non-1-ene (19), is of the same order of magnitude as that in transcyclooctene itself.

Prelog, Barman and Zimmerman postulated[23] that the normally parallel arrangement of the P_z orbitals on the sp^2 hybridised carbon atoms of an alkene might not pertain in a bridgehead alkene because of the steric constraints of the bicyclic system. Although maximum overlap of these P_z orbitals occurs when they are parallel, bonding is still possible even at fairly high values of the dihedral angle between these orbitals. Prelog et.al. proposed therefore that Bredt's rule was an example of steric inhibition of resonance of the two π electrons of a double bond and that in extreme cases such double bonds might show chemical reactivity reminiscent of diradical and/or dipolar forms.

Such twisting of p orbitals is only likely to be significant in transcyclo alkenes and, indeed, recent

X-ray studies have demonstrated that twisting exits in this type of compound, as exemplified by the cycloundecatriene humulene (22)[24] and the cyclodecatriene, germatriene (23)[25] where torsional angles of up to 20° have been observed.

Our objectives in embarking on a study of bridgehead alkenes were to test the Wiseman postulate; to determine the amount and type of strain involved in this type of structure; to study relative stabilities of such alkenes and to look in a qualitative way for evidence of abnormality in chemical reactivity and physical properties.

If Wiseman's postulate is correct, then alkenes of the type (24) should be capable of a separate existance. Examples of such compounds in the literature are rare. There are two cases known to us[26] where the compound (25) is claimed as a reaction intermediate and where it is claimed[27] that the compound (26) has been isolated. The latter seems the more likely, but the evidence is not conclusive, no spectral data being given. One of our synthetic objectives was, therefore, an olefin of this type (24), and for comparison purposes, we decided to prepare the isomeric type (27).

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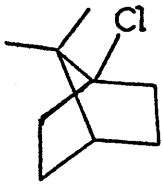

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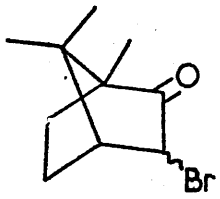

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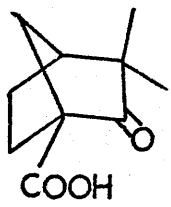

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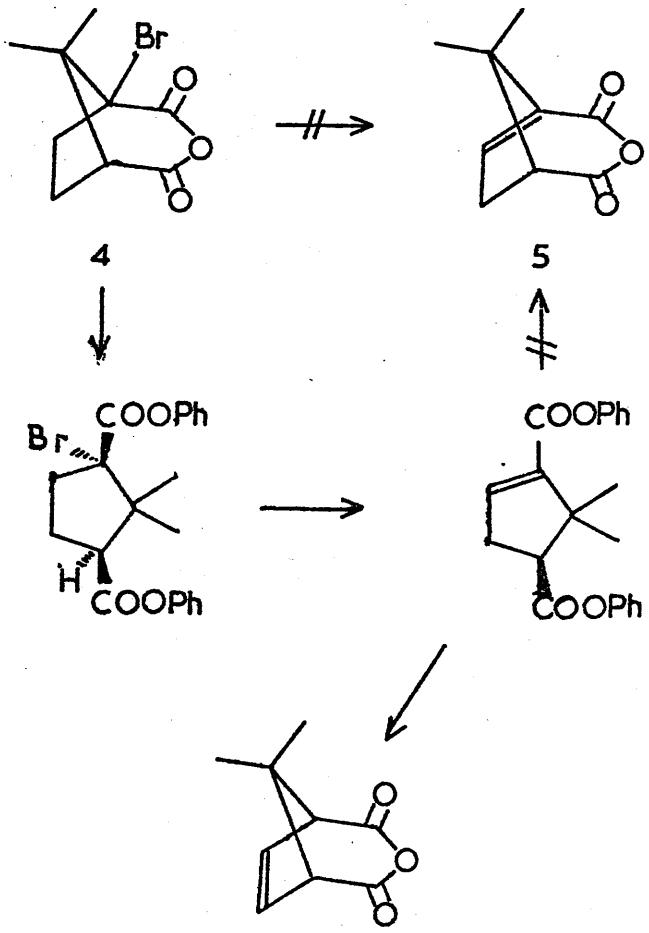
SCHEME I



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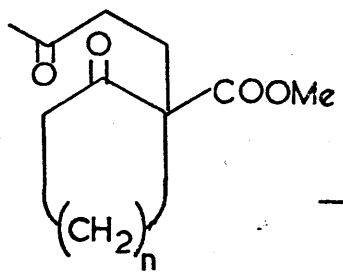

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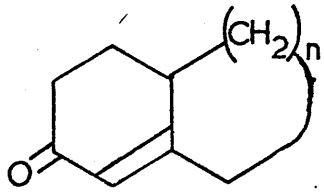

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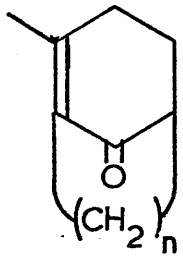
n= 3,4,[5].



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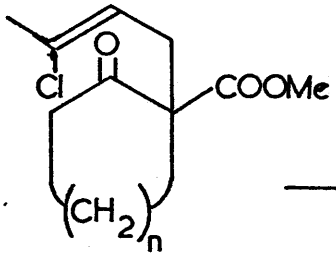
n= [5],6,7,12.



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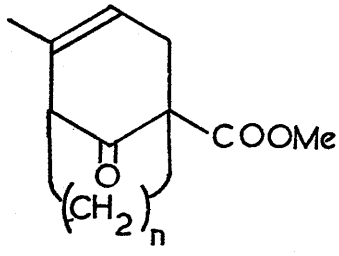
n= 3,4.



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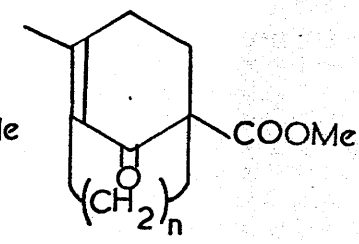
n= 5→10



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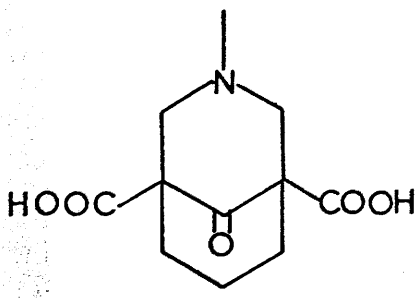

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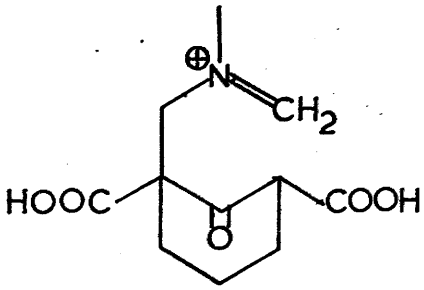

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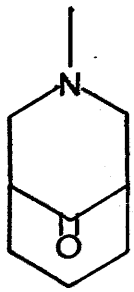

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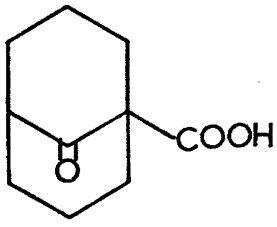

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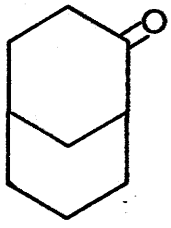

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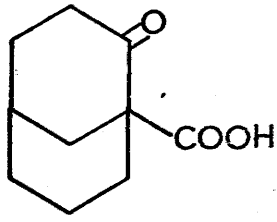

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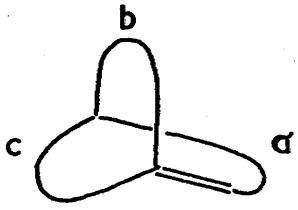

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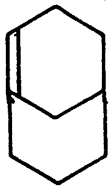

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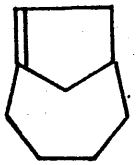

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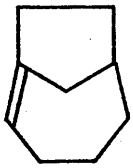

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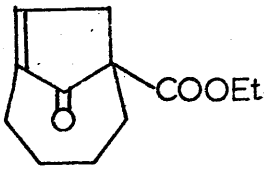

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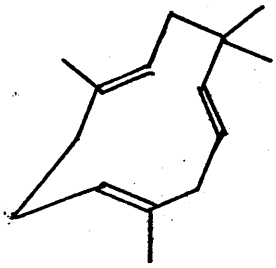

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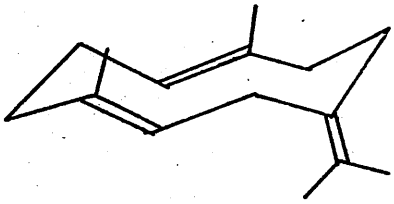

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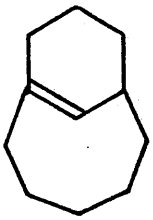

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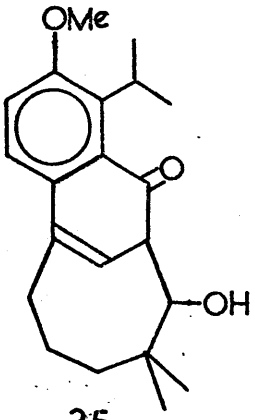

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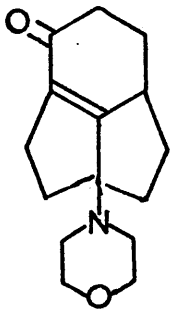

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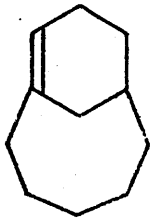

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D I S C U S S I O N

Part I

The Bicyclo (5, 3, 1) Undec-7-En-11-One System

In order to investigate the problems which are set out in the Introduction, we chose to make use of the bicyclo (5, 3, 1) undecane skeleton for two reasons. At the time of embarkation upon this research 8-methyl, 11-oxo, bicyclo (5, 3, 1) undec-7-ene (1) was the smallest and probably the most strained bridgehead olefin known[1]. It was easily accessible and seemed to be relatively stable. This would enable a study of the physical and chemical properties of bridgehead alkenes to be undertaken. We might also be able to obtain a suitable derivative for study by X-ray crystallography in order to gain some insight into the strain in the molecule and this information would be valuable in assessing the strain factors in other anti-Bredt olefins. A third reason for choosing the bicyclo - (5, 3, 1) - undecane system was not apparent until Wiseman[2] postulated that strain in anti-Bredt olefins is related to strain in trans-cyclo alkenes (see Introduction). The bicyclo (5, 3, 1) undecane system is the smallest bicyclic system, which, according to the Wiseman postulate, would tolerate a 1-branch olefin of the skeletal type (2). Anti-Bredt olefins of this type are unknown, although they have been postulated as reaction intermediates[3,4] and claimed as isolated products[5], in the latter case without much proof.

We chose to study enones rather than alkenes because the former were more convenient for the study of physical and chemical properties. In addition we expected to be able to use physical methods to investigate the extent of conjugation in the system. From the work done by Prelog[6] it was known that in bicyclo (n, 3, 1) alkenones of the type (3), as n decreases the conjugation of the enone system becomes poorer, as evidenced by a systematic lowering of ε as n decreased from 12 to 5. (Table I). This can be rationalised by an examination of molecular models, when it becomes apparent that as n decreases, the angle between the planes, defined by the alkene and carbonyl functions, increases, thereby introducing steric inhibition of resonance. That this phenomenon has a pronounced effect on the ε value of chromophores is well established[7], but the existing semi-empirical relationship[7] between ε and the angle of twist has never been rigorously tested. One further advantage in studying enone systems rather than alkenes is that resonance energy might help to stabilise the compound (4) which was ultimately sought as a test of the Wiseman postulate, since examination of a molecular model indicated that this enone system might well be planar. The one criticism that we had of studying the enone

systems, was that these conjugative energy factors might distort the relative stabilities of the parent alkene moieties, but since this aspect was already qualitatively understood, we were not unduly concerned about this aspect of the subject.

In order to obtain the simple enone (5), the following synthesis was undertaken. (see Scheme I). Cyclooctanone was converted to the β keto-ester by reaction with diethyl carbonate and this product was readily converted to the aldol (7), by addition of acrolein and ring closure of the intermediate aldehyde (6). Difficulty was being experienced in dehydrating the aldol (7) when the method of Warnhoff[4] was published achieving this step in 73% yield. The enone-ester (8) synthesised in this way was hydrolysed to the acid (10) and decarboxylation of this acid to a mixture of the enones (5) and (12) was achieved in 68% yield by the method of Prelog[1], using refluxing quinoline. The enone (5) so obtained always contained ca. 7% of the βɣ enone (12) and was therefore of little use for further study, since separation was achieved only by preparative g.l.c. and interconvertion of the two isomers occurred very readily.

However, the mechanism of this decarboxylation was

of interest to us, since the reaction conditions used were such that equilibration between the αβ and βγ enones could conceivably occur. It was possible to visualise two mechanisms :

a) decarboxylation of the βγ enone acid (11) followed by re-equilibration of the enone system.

b) direct decarboxylation of the αβ enone acid (10). If the latter mechanism was operative it would involve an intermediate of the type (13), containing two bridgehead double bonds. On the other hand, decarboxylation of (11) would involve a less strained transition state. That the αβ rather than βγ enone acid was decarboxylating was indicated by the ratio of αβ to βγ enone in the product. This ratio was found to be 93:7 whereas the ratio of (5) to (12) at equilibrium was found to be 75:25. Hence the equilibrium was being approached from the side of the αβ enone, implying that the αβ enone was the kinetic product of decarboxylation.

It is interesting to note that in the enone-ester series the equilibrium ratio of αβ enone (8) to its βγ isomer (9) was found to be 90:10, whereas in the parent enone series it was found to be 75:25. This may be due to subtle effects in the conformation[8], caused by bond angle changes introduced by the carbethoxyl substituent. The

observed difference in equilibrium ratio between the two series, served to emphasise that a study of the simple enone (5) rather than the enone-ester (8) was advisable if any meaningful conclusion were to be drawn.

Although the enone-ester (8) was a poor source of pure enone, it provided a convenient source of a derivative for examination by X-ray crystallography. Our first attempts involved convertion of the enone-ester (8) to the diol (14) by LAH reduction, followed by selective oxidation of the allylic alchol to the keto-alcohol (15). Several unsuccessful attempts were made to prepare a suitably crystalline derivative of this compound, but finally the parachloroanilide derivative (16) of the acid (10) was found to be suitable for analysis by the X-ray method.

The crystals of (16) are orthorhombic, space group P_{bca}, Z=8, a = 19.97, b = 7.67, c = 21.35Å. 983 Independent structure anplitudes from the reciprocal lattice nets h, 0→8,1 were recorded on a Hilger and Watts linear diffractometer using Mo-Kα radiation (λ = 0.7107Å). The position of the chlorine atom was found by Patterson methods and after initial difficulties involving pseudo-symmetry in the unit cell the remaining atoms were revealed by subsequent electron-density calculations. The atomic parameters were refined initially by full matrix

and subsequently by block diagonal, least squares methods to a final value of R = 0.092. The data obtained from this analysis are shown in tables 2 and 3 together with a view of the molecule down the b crystal axis.

Geometric constraints cause the C = O to be twisted by 37.7° about the C(7) - C(11) bond, as seen, (17A), by comparing the planes defined by C(6) - C(7) - C(11) and by C(7) - C(11)-O. The C(7) - C(8) double bond is also twisted by 8.6° as seen by comparing the plane through C(7) - C(8) - C(9) with that through C(6) - C(7) - C(11) (17B). Thus the non-planarity of the enone system is less marked at C(8) than at C(7), but the overall effect is an αβ enone which is little better than 'half conjugated'. Deconjugation also affects bond lengths (Table 2) and the C(7) - C (8) bond length of 1.29Å is virtually that of an isolated double bond, when compared with the corresponding data derived from X-ray analysis[9] of the fully conjugated, planar cyclohexenone, ecdysone. The C(7) - C(11) bond length (1.48Å) is as long as the C(1) - C(11) bond (1.49Å) and thus practically that of a pure single bond. A comparison of the bond lengths found in the molecule (17) with those of a fully conjugated cyclohexenone system, as found in ecdysone, is presented in Table 4. The estimated standard deviation in measurement of a C-C being 0.02Å, the

tabulated values are accurate to within $\mp$ 0.06Å and although the outer range of the error limits brings them near to normality, they remain just significant. This implies that the canonical forms (18) and (19) contribute little to the enone system in this case. It is now possible to identify the types of strain present in bridgehead olefins as :

i) warping of the olefinic bond

ii) bond angle deformation

Although the former is believed[10] to produce 0.5 Kcal./mole of strain, the effect of the latter is only qualitatively understood. Some insight into the effects of alkene warping can be obtained from the graph (1), derived from the results of Sutherland et.al., which shows how strain increases as warping becomes more pronounced. No such quantitative relationship exits between angle (Baeyer) strain and strain energy. Allinger has calculated[11] that an expansion of 4^{o} in all of the C-C-C bond angles of cyclo octane raises its energy by 0.28k cal/mole, but this increase in valence bond angle lowers the overall enthalply of the molecule by producing improvements in various dihedral angles. Thus, deformation of valence bond angles is only one component of ring strain (I strain), to which other factors such as Pitzer and transannular interaction strains also contribute. These components of

ring strain are not mutually independant[12] and their individual contributions cannot be estimated with certainty. One further type of enthalpy increasing deformation which may be present in bridgehead alkenes, is the double bond bending type (20) postulated[13] by Schleyer. A search is being made for this type of deformation in the derivative (16), but results are not yet to hand.

Since the enone (5) was obtained together with its βɣ isomer from the decarboxylation reaction, an alternative synthetic route to this enone was sought. A careful search of the literature revealed few papers on the bicyclo (5,3,1) undecane skeleton but one paper[14] came to light which reported that, "attempts to obtain acid (25) via fragmentation of keto tosylate (24) using potassium hydroxide in dioxan or methanol were unsuccessful. An unsaturated cyclo octanone (presumably 12) was obtained instead". The evidence for (12) was the appearance of two n.m.r. signals at δ6.05 and δ5.73 (no integration reported) attributed to the vinyl protons. We were somewhat puzzled over the origin of this compound. It is to be expected, from its mode of formation, that the tosylate function is equatorial, and as Martin and Parker have shown[15], an elimination leading to the enone could only take place under the most drastic conditions, and then only if the six-membered ring adopted the boat conformation (Scheme 3,

mechanism A). A more likely event was nucleophilic attack on the carbonyl function, followed by bridge-scission (Scheme 3, mechanism B). If on the other hand, the tosylate function was axial, the reaction conditions employed were unusually mild. It was decided to repeat the synthesis of the keto-tosylate (24), to determine its stereochemistry and to carry out the base treatment using sodium ethoxide in ethanol, a method[15] which was well established in this department. The dione (21), which was prepared by the literature route[14], was converted to the keto-tosylate (24) by Marshall's method as shown in scheme 2. Ethoxide treatment gave as the kinetic product, a compound which had most of the characteristics expected of the enone (5). The product had λ_{max}^{EtoH} 238 (ε = 5,630) and showed a signal in the n.m.r. at δ6.16. Prolonged reaction times (40 hours) produced a 75:25 mixture of this enone and another, isomeric compound, presumably (12). An exact replica of Marshall's experiment was performed, in which a ratio before distillation, of 98:2 of $\alpha\beta$ to $\beta\gamma$ enone was obtained. Marshall's result may be explicable by equilibration of the products by unremoved base during distillation. In this event a ratio of 75:25 of the $\alpha\beta$ to $\beta\gamma$ enones would be obtained.

The n.m.r. spectrum of a 4:1 mixture of these two enones shows integrated intensities for the vinyl protons

at δ6.15 and δ5.7 in the ratio of 2:1, due to there being 2 vinyl protons per molecule of (12) but only 1 vinyl proton per molecule of (5). This partial explanation of Marshall's result is not however, wholly satisfactory. The mechanism of the reaction (24) → (5) was of some interest to us and three possible mechanisms were considered. These are shown in scheme 3. The fact that the tosylate function was equatorial was deduced by the n.m.r. method[16] of Hassner. The band width at half height ($W_{\frac{1}{2}}$) of the C-8 proton signal of keto-tosylate (24) is 17Hz., within the range $15 < W_{\frac{1}{2}} < 30$ quoted by Hassner[16] for an axial proton. Moreover, the kinetic product was the αβ enone (5) as evidenced by the fact that the reaction mixture, when examined ca one minute after the addition of base contained less than 2% of the βɣ enone but after 40 hours contained 20%. Since (5) is the kinetic product mechanisms A and B can be discounted, leaving mechanism C, which can be regarded as an E_{1cb} elimination[17] (C(i) → 5) or as a fragmentation[18] (C(ii) → 5). One factor in favour of mechanism C(ii) is that it fulfills all the geometric requirements for a 'frangomerically assisted' fragmentation and fits well with the observed reaction speed, sodium toluene-p-sulphonate being visibly precipitated immediately upon addition of the base.

Having established a high yield route to pure enone (5),

we began to examine its physical and chemical properties.

The first of the physical properties to be examined was the ultraviolet spectrum. A comparison of the λmax and ε values of the enone (5) with those of a model system (2 methyl cyclohexenone), the enone moiety of which is known to be planar, is shown in table 5. The position of the λmax value is indicative of the energy difference between the highest occupied molecular orbital and the lowest unoccupied molecular orbital. The argument of Braude[7] leads one to believe that the energy difference between these two levels in the bicyclic enone is 3 n.m.(or ca 1.8 Kcal/mole) smaller than in the model system. The relationship between the ε value and the interplanar angle, which has been introduced by Braude is $\varepsilon / \varepsilon_o = \cos^2\theta$, where ε is the extinction coefficient of the non-planar system, ε_o is the extinction coefficient of a model, planar system, and θ is the interplanar angle between the two parts of the chromophore. An application of this relationship to the bicyclic enone yields a value of $\theta = 41.5^\circ$, which is remarkably close to that found experimentally ($\theta = 37.7 \pm 1^\circ$). Braude's $\cos^2\theta$ relationship has recently been questioned[19], the questioners preferring a simple $\cos\theta$ relationship, but application of the equation $\varepsilon/\varepsilon_o = \cos\theta$ in the case of the enone (8) gives $\theta = 55.1^\circ$. Thus, in this, the first case in which Braude's relationship could be put to the test, it seems that the use of $\cos^2\theta$ is to be preferred to the use of

$\cos\theta$ alone.

The next physical property which was examined as a probe to molecular distortion was nuclear magnetic resonance. In a non-planar enone such as (5), any contribution to the wave function from the canonical form (18), would be small. This should result in the β-carbon atom of the enone system carrying less positive charge than does the β-carbon atom of a planar enone, thus causing the ^{13}C chemical shift to be at lower field than in the corresponding planar enone. That the effects produced by non coplanarity are large compared with other factors has been shown[20] by Stothers.

The difference in charge density at the β carbon atom can also be seen, as a secondary effect, by observation of the chemical shift of the β hydrogen atom. Since ring size has a pronounced effect[21] on the chemical shift of the β hydrogen of an enone system, 2 methyl cyclohexenone was again chosen as a suitable model for comparison. A comparison of the resonance frequencies of the β hydrogen atoms in these two molecules (Table 6) shows that the β hydrogen of the bicyclic enone resonates at higher field, reflecting the difference in charge density. That this difference is due to decreased conjugation and to no other effect, is shown by the fact that the vinyl hydrogen atom in each of the derived allylic alcohols shows the same chemical shift value. A semi-quantitative treatment of the effect

of substituents and their orientation, on the chemical shift of vinylic hydrogens has been given[22], but since it takes no account of molecular distortion, the calculated and observed values are, as expected, at variance (see Table 6).

Infra-red spectroscopy is of little value as a method of detecting twist because of the pronounced effect[23] produced on the ν C = O by relatively small deformations of valence bond angle. As was seen from the results of the X-ray analysis, the carbonyl angle (112.7°), is not that normally found in a cyclohexenone (118°), this small difference being capable[23] of producing a shift in ν C = O of ca 10cm.$^{-1}$. Consequently, the data obtained on enone (5) cannot be meaningfully interpreted.

There remains one further method which could be of considerable utility in determining the extent of twist, not only in enones, but even in the alkenes themselves. If the racemic products of synthesis could be resolved into their d and l forms by complexing them with some suitable reagent[24] they would then be susceptible to analysis by the optical rotary dispersion method[25] of Snatzke. This method has recently been used by Sicher[26] to study the chiral olefin tricyclo (4.4.0.$0^{3,8}$) dec-4-ene. ('Twistene') a molecule with a torsional angle of ca 20°. We now investigated the chemical properties of the enone to discover

how these are affected by the strain in the molecule. The strain has been found to be of two types :

a) π -bond twist

b) poor conjugation

In view of the currently accepted mechanism of epoxidation of an $\alpha\beta$ enone by alkaline perhydrol (scheme 4), which demands a double bond between the oxygenated and α carbon atoms (scheme 4(ii)), it would be expected that strain of type (b) would disfavour this reaction. In view of the fact that high electron density within a C = C is essential to epoxidation by per-acid the same factor should facilitate epoxidation by this route, and moreover the rate of epoxidation by peracid will be further enhanced[10] by strain of the type (a).

Using alkaline perhydrol conditions under which isophorone is epoxidised in 72% yield in 4 hours, the enone (5) was ca 50% (G.L.C.) converted after 3 days. Using metachloroperbenzoic acid in chloroform as reagent, the enone (5) was quantitatively converted to its epoxide in one week. This behaviour is less striking than was expected but is consistant with an enone which is poorly conjugated, and the alkene moiety of which has a decided twist.

Further evidence of poor conjugation was obtained from the fact that diethyl malonate gave no Michael adduct after 4 hours (G.L.C.) whereas cyclohexenone gave a 90% yield of adduct in 6 hours under identical reaction conditions[28].

An attempt to detect pure alkene character in the enone (5), by preparation of a 2,4, dinitro sulphenyl chloride adduct[29] was unsuccessful, due to equilibration of the substrate under the reaction conditions and addition of reagent to the βδ enone produced by equilibration.

Part II

The Bicyclo (5, 3, 1) Undec 7-(11) ene 8 one System

The synthesis of an alkene of the type(2)was now undertaken and several different methods were attempted. It was considered (scheme 5), that pyrolysis of the quaternary ammonium hydroxide (29) utilising a (trans) Hoffmann elimination or of the amine oxide (30) using a (cis) Cope reaction might be achieved, depending on which of the C - 11 stereoisomers of (28) was available. It was intended to prepare the amine (27) by hydride reduction of the oximino-ketone (26). The stereochemistry at C - 11 in (27) would be established by the n.m.r. method described on page 33

The allylic amine (27) would then be hydrogenated to the saturated analogue (28) followed by conversion to (29) or (30). Quantitative conversion of the enone (5) to its oximino derivative (26) was effected with hydroxylamine hydrochloride in ethanolic sodium hydroxide solution to yield a mixture of the syn- and ante-oximes (26). These oximes could not, however, be reduced to the allylic amine (27), even with lithium aluminium hydride in refluxing 1,2 dimethoxy ethane. This method was therefore abandoned.

A second route envisaged the use of a reaction (31→32), recently described by Wharton[44,45]. However, attempted rearrangement of the αβ epoxy-ketone (33) in this way, even under the most vigorous conditions, gave none of the expected product (34) (t.l.c./g.l.c.), starting material being recovered.

Another reaction which seemed applicable and which proceeds stereospecifically under mild conditions, is that described by Whitham[30], in his synthesis of transcyclooctene (36) from the transdiol (35). In the present case (scheme 6) we made use of the aromatic enone (38), which was prepared[31] from (37) as an inseperable mixture of (38) and (39). Epoxidation of this mixture afforded (40) and (41). These could be separated and reduction of the former yielded (42), but an attempt to prepare the acetal (43) was fruitless. The two epoxy ketones (40) and (41) were identified spectroscopically (see Experimental). Further attempts to prepare (43) were not made because of the scarcity of material, since the diol (42) was derived from the enone (38) which made up only 20% of the mixture of enones (38) and (39) at equilibrium.

During the repetition of Marshall's synthesis[14] of the keto-tosylate (24) (see Part I), a spectral examination of the diketone (21) was undertaken. The data obtained is shown in table 7, together with comparative figures for two similar diketones. It can be seen that each of the three diketones shows the expected doublet in the C=O region and that the two model compounds show almost constant values of $\nu_2 - \nu_1$ and of $\varepsilon a_1/\varepsilon a_2$, whereas the dione (21), although showing a relatively constant peak separation ($\nu_2 - \nu_1$) has

variable ratio of εa values. When neither $\nu_2 - \nu_1$ nor the εa ratio changes with solvent polarity the splitting of the $\nu C = O$ has been attributed[32] to a dipole/dipole interaction, but when both of these quantities change with solvent polarity the phenomenon has been attributed[33] to Fermi resonance. In the present case, since the observed behaviour obeys neither of these sets of conditions, an explanation other than Fermi resonance or dipole/dipole interaction must be sought. One possible explanation is that in polar solvents, the diketone (21) contains a small proportion of one enol form, causing one carbonyl band to decrease in intensity relative to the other. It is the higher frequency band which decreases relative to the lower frequency band and since the former has been assigned[14] to the C - 8 carbonyl function, this would seem to imply the presence of an enol of the type (44). However, the basis for this assignment is very slender. An alternative, (45), is also possible as is an unequal mixture of (44) and (45).

Further evidence of enolisation was obtained from the U.V. spectrum of (21). When the U.V. spectrum of this diketone was run in hexane, it showed no sign of enolisation, exhibiting only end absorption. However, when the spectrum was run in ethanol, a strong maximum could be seen at 268 nm., as well as the end absorption. When base was added, in addition to the band at 268 nm., a further maximum which could

be due to enolate anion appeared at 315 nm.

If the diketone (21) exists in alcoholic solution as a mixture of the enols (44) and (45) it would be of interest to trap the enols as enol-ethers using diazomethane under neutral conditions and as enol-acetates using isopropenyl acetate under acidic conditions in an attempt to measure the free energy difference between the two enol forms. The conjugative energy parameters, introduced by the presence of the carbonyl functions, prevent any $\Delta F^{\ddagger}$ determined in this way from reflecting accurately the relative stability of the two alkenes (2) and (46). These parameters should favour the enol of the type (45) since an examination of molecular models indicates the possibility of good conjugation in an enone of this type.

In the event, two products were isolated from the diazomethane reaction and were subsequently identified as the enolether (47) and the C-methylated diketone (48). This latter product must have arisen from charge density on C - 7, a phenomenon not unknown[34] in such reactions. That these compounds had the structures allocated to them was proved by synthesis of (47) by an alternative route (see below) and by comparison of the n.m.r and i.r spectra of (48) with the literature[14] values.

Attempts to isolate the enols as their acetates under thermodynamic conditions, by the method of House[34], yielded

only one enol-acetate formulated as (49). These findings may mean that only one enol, (44), is present and/or that steric factors hinder approach of reagent to the C - 11 oxygen.

Since the two products obtained from the reaction of diazomethane with the diketone(21) were separable only with difficulty, a new route to the enol ether (47) was sought. Utilising the fact that the C - 8 carbonyl of the diketone (21) was more reactive than its counterpart at C - 11, the C - 8 dimethyl ketal (50) was prepared (scheme 7). As expected, the free ketonic function in (50) is very hindered and this compound was recovered unchanged from attempted hydride reduction or phenyl magnesium bromide addition. Acid catalysed pyrolysis of the ketal (50) yielded a 55:45 mixture of the two enol-ethers (47) and (51) which show the expected spectral characteristics. This result not only provided a synthesis of the diazomethane product (47), but also a starting material for the synthesis of enones of type (52). The mixture of enol ethers (47) and (51) reacted with phenyl magnesium bromide yielding one product only which had all the spectral features expected of the enol-ether/alcohol (53). Thus it would seem that removal of the small amount of conjugative energy conferred by the C - 11 carbonyl causes the double bond to migrate away from the bridgehead position. Hydrolysis of this compound with methanolic toluene-p-sulphonic acid yielded the enone (52). This phenyl enone showed all of

properties normally associated with a planar, conjugated molecule of the benzalacetone type. These are quoted in tables 8 and 9, together with the corresponding data on the isomer (38)[31] and other related systems. Unlike the enone (52), the isomer (38) had the peculiar features exhibited by a non-planar enone system. Photographs of molecular models of these two molecules showing the non-planar enone chromophore of (38) and the planar chromophore of (52) are shown in figures 1 and 2.

Encouraged by this success our attention was then focussed on the synthesis of the parent enone (4), by hydride reduction of the enol-ethers (47) and (51). A knowledge of the stereochemistry of this process was of the greatest importance in planning the type of elimination (54 → 4) to be used. A study of this reaction was therefore undertaken on the model system (5). That hydride reducing agents approached these alkenones in such a way as to produce only one of the two possible epimers at C - 11 was shown by g.l.c. analysis. The single epimer produced was shown by n.m.r. spectroscopy to be that in which the hydroxyl function was equatorial in the six-membered ring. By irradiating the signal due to the vinylic hydrogen and observing the signal due to the carbinyl proton, a coupling of 2.5 Hz between these two atoms was seen to collapse, indicating that the atoms are related as in (55a) and not as in (55b). In these

epimers the coupling constants would have been expected[35] to be ca 3Hz and Ca 0 Hz respectively.

It was found that the mixture of keto-enol-ethers (47) and (51) was readily reduced by lithium aluminium hydride to give only one of the two possible epimeric alcohols at C - 11 (g.l.c/T.L.C). Again it was noted that the product isolated at this stage was the hydroxy/enol-ether (56), the double bond having migrated out from the bridgehead. We assume the stereochemistry shown (56) by analogy with the model systems studied and also by the absence of any OH → π bonding. It has been shown[36] that systems of the type (57) show OH → π bonding, and since this was not apparent in the i.r. spectrum of (56) the stereochemistry is assumed to be as shown. Very mild acid hydrolysis of (56) gave the required ketol (54) which initially gave one peak on g.l.c. analysis, but an undistilled sample which was allowed to age for 3 days showed signs of a second peak of shorter retention time. Spectroscopic data are consistant with it being the C - 11 epimer (58) of the originally formed ketol, i.e. in the i.r. spectrum of this aged sample the originally sharp hydroxyl band was found to have broadened and fine structure began to appear to the low frequency side of the carbonyl band. This was consistant with the possibility of hydrogen bonding in the epimer (58a). The epimerisation can be simply explained as in scheme 8. That epimerisation had not occurred during

hydrolysis was shown by an examination of the n.m.r. coupling constant of the carbinyl proton. A full interpretation of the n.m.r. signal due to this proton in the pure epimer originally obtained is not possible[37] since this signal is the X part of an ABX spin system, the A and B components of which are hidden, but from the size of the coupling observed ($W_{\frac{1}{2}}$ = 14Hz) it seems reasonable to assume that the hydroxylic function is equatorial.

Attempts to dehydrate the ketol (54) directly, using dilute sulphuric acid, toluene-p-sulphonic acid in either benzene or toluene, thionyl chloride or amine salts yielded in each case a plethora of products, none of which showed the spectral properties expected of the enone (4).

Since it was obvious that direct elimination of the hydroxyl group was not feasible, a mesylate derivative (59) was prepared after some initial difficulty. We now attempted to bring about a Grob fragmentation of the keto-mesylate (59) as shown in (60), by base treatment. In fact the reaction of (60) with sodium methoxide in methanol, conditions which had been successful in fragmenting (24) to (5), yielded only the β methoxy ketone (61). This product could well arise by S_N2 displacement of mesylate or by elimination (59→4) followed by addition of methanol.

The enone (4) was finally obtained by treatment of the oxo-mesylate (59) with refluxing anhydrous N,N-dimethyl

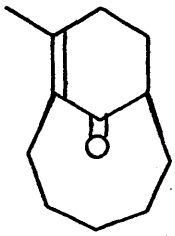
formamide. Yields were generally poor and speed of work up was critical, for, on standing, the enone rapidly decomposed to form a grey solid mp 108 - 110°, showing $\nu_{C=O}^{NUJOL}$ 1710 cm^{-1}, which is probably a dimer. A high yield route from oxomesylate to enone (4) was eventually obtained. Treatment of the oxomesylate (59) with the strongly basic but non nucleophilic organic base, 1, 5 diazabicyclo (4.3.0) nonene 5, effected the desired fragmentation and gave the enone in 52% yield, as a low melting, volatile solid.

Although the enone (4) is isomeric with that enone (5) already described, its mass, infra-red, ultra-violet and n.m.r. spectra show radical differences. The $\Delta^{7,(11)}$ enone shows all the features of a full conjugated chromophore as evidenced by $\nu_{C=O}^{CCl_4}$ 1675 cm^{-1} in the i.r. and a chemical shift value of the β hydrogen atom of the enone at δ6.85 in the n.m.r. A comparison of the properties of the two enones (4) and (5) is presented in table 10.

CONCLUSION

The synthesis of the enone (4) represents the first synthesis of a 1-branch bridgehead alkene contained in a bicyclic system, and further confirms the validity of the Wiseman postulate. The isolation of enol derivatives of only the Δ^7 type from the diketone (21) indicates preferential enolisation to the Δ^7 rather than to the $\Delta^{7,11}$ form, with the proviso that it may also be a reflection of the ease of reagent attack at C-7 and C-11. That the $\Delta^{7,11}$ isomer is of higher enthalpy than the Δ^7 isomer is evedinced by the larger bathochromic shift(ca 20nm.) in the u.v. spectrum of the former than in the latter(ca 3nm.), this shift being caused by a twisting of the 'p' orbitals of the alkene from the preferred parallel arrangement. bond twisting of this type, together with deformation of bond angle has been the main strain accommodating deformation found in an X-ray structure analysis of a derivative of the Δ^7 enone. No systematic study of the relative stabilities of the two enones (4) and (5) has been undertaken but it has been noted that enone (4), which was expected to be less stable, decomposed much more rapidly than its isomer (5). A systematic study of the chemical reactivity of enone (5) leads to the conclusion that it behaves as an enone which is ca 50% conjugated. Abnormality of u.v., i.r. and n.m.r. spectra have been observed for the enones (4) and (5), but the most meaningful data has been derived from the u.v. spectra, this data being qualitatively

supported by the n.m.r. results. I.r. spectroscopy has proved to be of little utility due to the presence of bond angle deformations.



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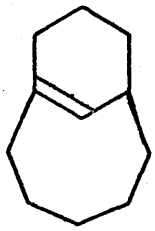

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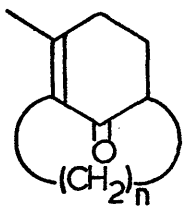
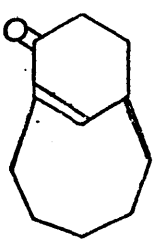


3

TABLE I

n	$\lambda_{max.}^{EtOH}$ (nm)	Log ε
5	251	3·80
6	251	4·00
7	251	4·10
10	250	4·10
12	250	4·15



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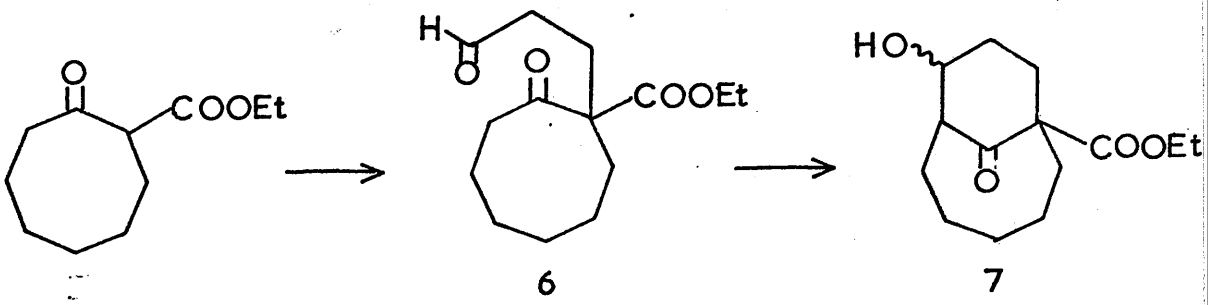
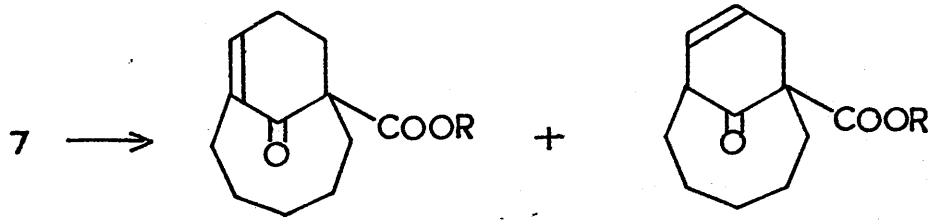
SCHEME I

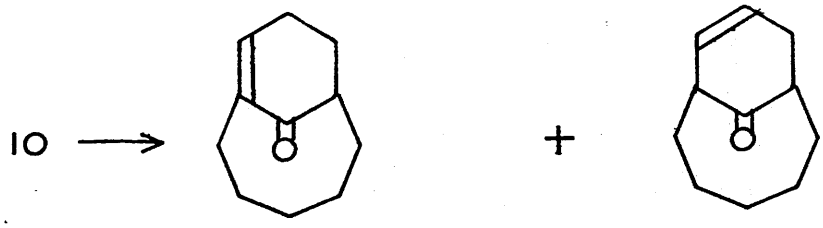


6 7

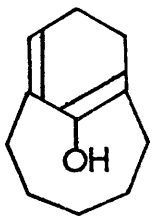


8 R=Et 9 R=Et

10 R=H 11 R=H



5 12



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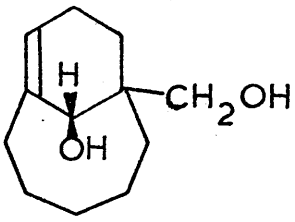

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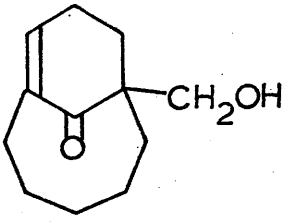

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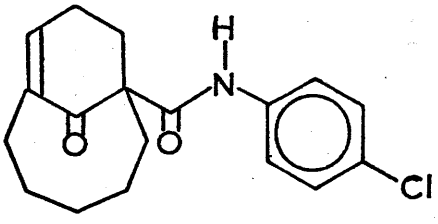

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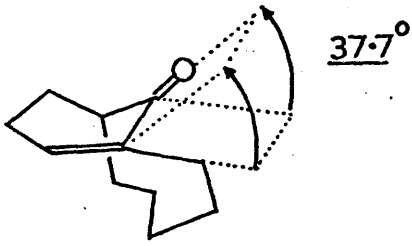
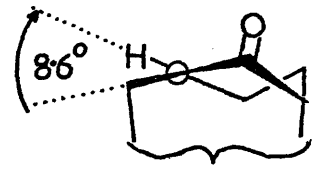
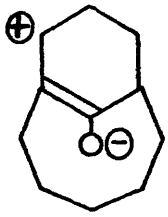


17A



VIEW ALONG C(7)-C(8) BOND

17B



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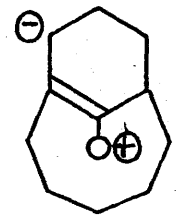

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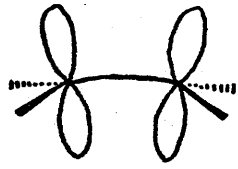

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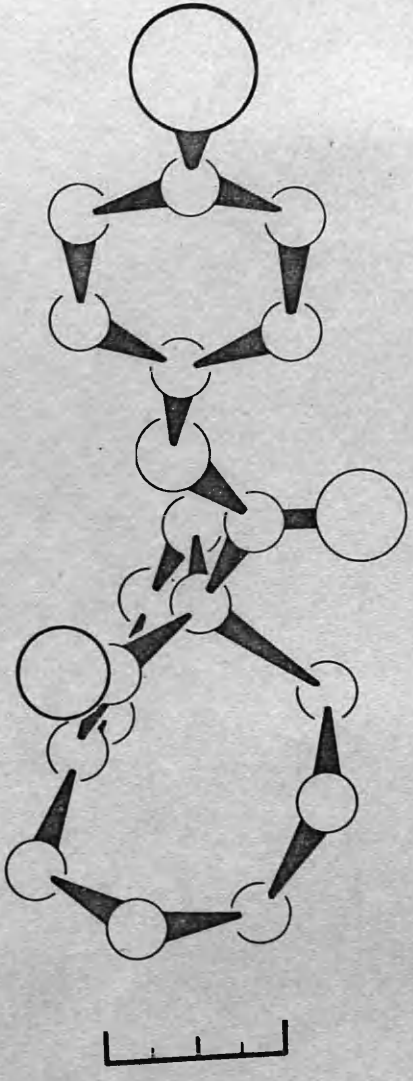


TABLE 2 BOND LENGTHS

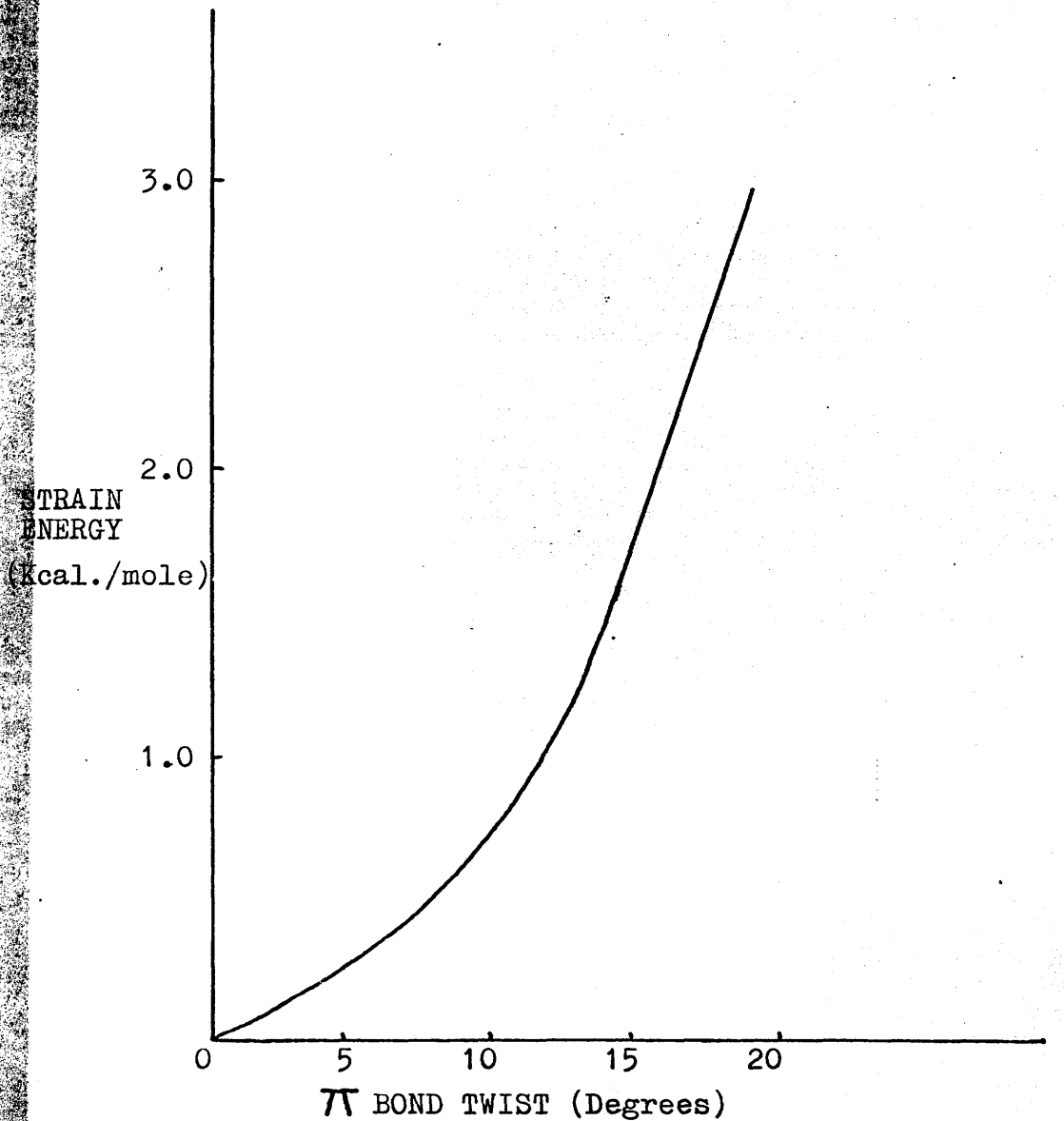
SINGLE BONDS		DOUBLE BONDS	
C(1) -C(2)	1.56	C(7) -C(8)	1.29
C(2) -C(3)	1.56	C(11)-O(19)	1.23
C(3) -C(4)	1.57	C(12)-O(20)	1.19
C(4) -C(5)	1.51		
C(5) -C(6)	1.56		
C(6) -C(7)	1.53		
C(7) -C(11)	1.48		
C(8) -C(9)	1.50		
C(9) -C(10)	1.56		
C(10)-C(1)	1.57		
C(11)-C(1)	1.49		
C(12)-C(1)	1.53		

TABLE 3 BOND ANGLES

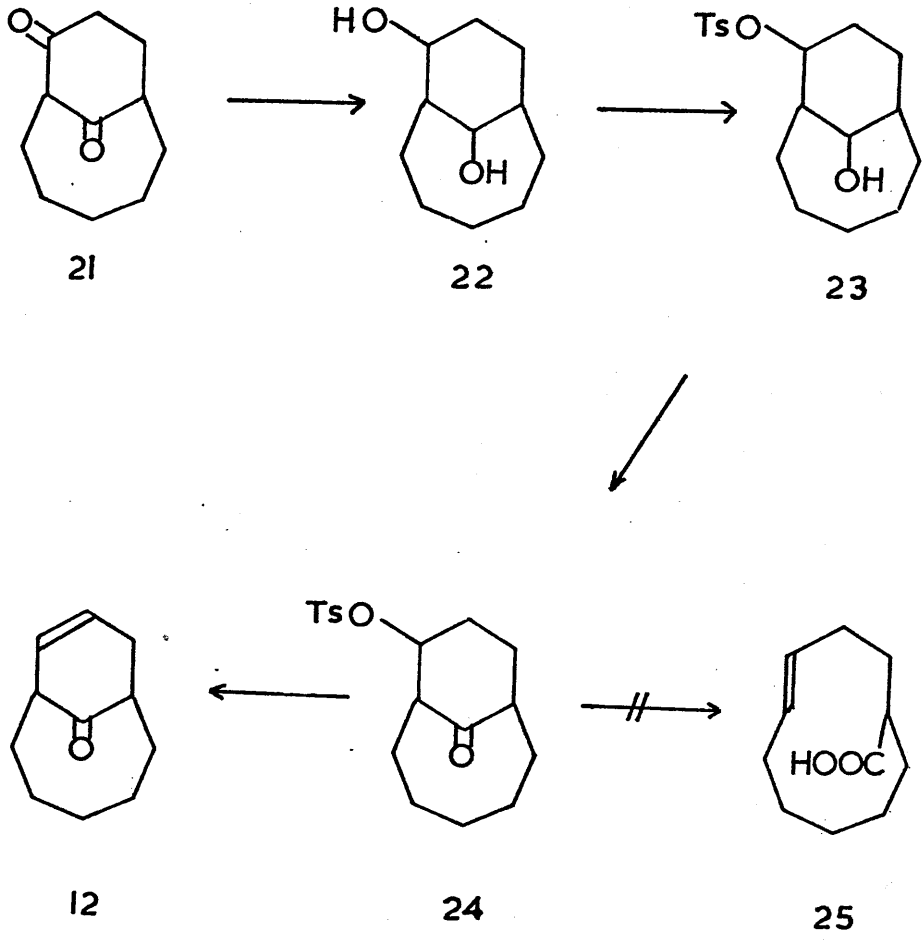
sp^3 ANGLES		sp^2 ANGLES	
C(1) -C(2) -C(3)	113.1	C(6)-C(7) -C(8)	125.8
C(2) -C(3) -C(4)	117.1	C(7)-C(8) -C(9)	125.4
C(3) -C(4) -C(5)	117.1	C(6)-C(7) -C(11)	113.5
C(4) -C(5) -C(6)	114.5	C(8)-C(7) -C(11)	120.1
C(5) -C(6) -C(7)	111.1	C(7)-C(11)-O(19)	122.7
C(8) -C(9) -C(10)	112.9	C(1)-C(11)-O(19)	124.4
C(9) -C(10)-C(1)	112.8	C(7)-C(11)-C(1)	112.7
C(11)-C(1) -C(2)	108.5		
C(10)-C(1) -C(11)	106.2		
C(2) -C(1) -C(12)	108.9		
C(10)-C(1) -C(12)	107.5		

TABLE 4 COMPARISON WITH A NORMAL CYCLOHEXENONE

BOND	IN(17)	IN BODYSCONE	ANGLE	IN(17)	IN BODYSCONE
C(11)-O(19)	1.23	1.25	C(1) -C(11)-C(7)	112.7	118
C(11)-C(7)	1.48	1.43	C(11)-C(7) -C(8)	120.1	122
C(7) -C(8)	1.29	1.35	C(7) -C(8) -C(9)	125.4	124
C(8) -C(9)	1.50	1.52	C(8) -C(9) -C(10)	112.9	111
C(9) -C(10)	1.56	1.56	C(9) -C(10)-C(1)	112.8	110
C(10)-C(1	1.57	1.53	C(10)-C(1) -C(11)	106.2	111
C(1) -C(11)	1.49	1.52	C(1) -C(11)-O(19)	122.7	119
			C(7) -C(11)-O(19)	124.4	123

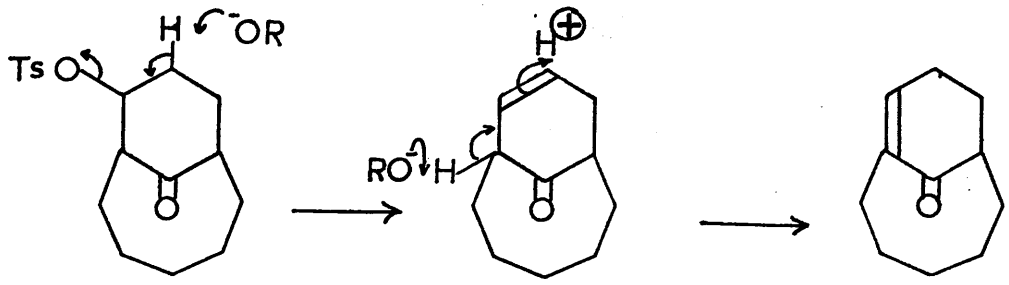

3.0
2.0
1.0
STRAIN
ENERGY
(Kcal./mole)
0
5
10
15
20
π BOND TWIST (Degrees)

SCHEME 2

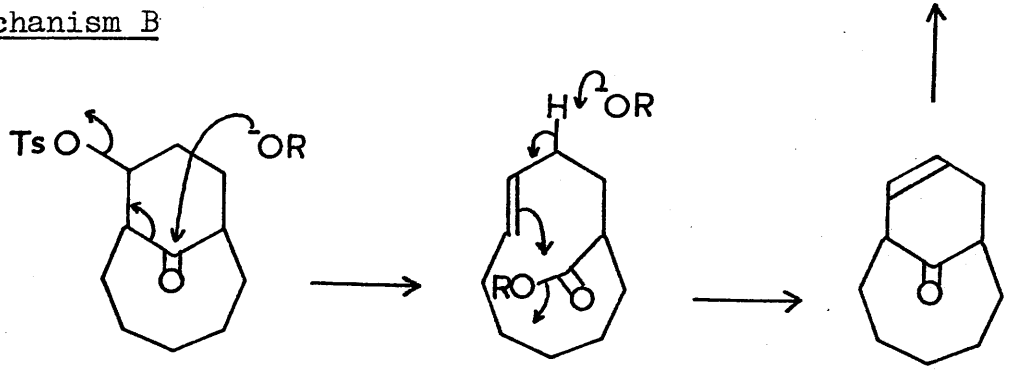


SCHEME 3

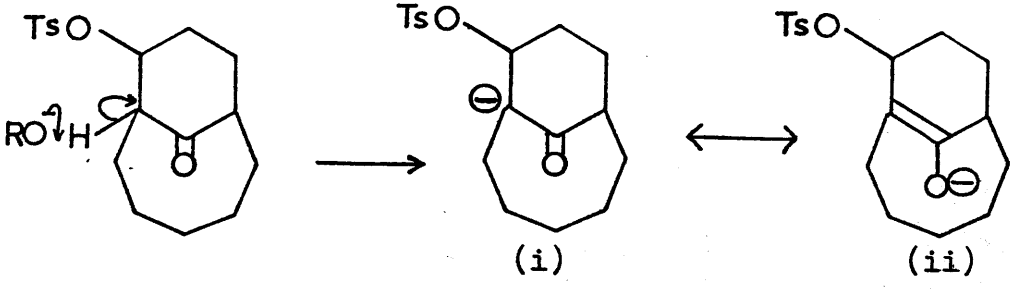
Mechanism A

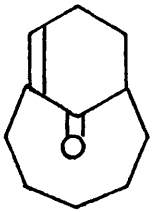
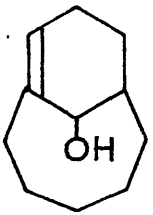
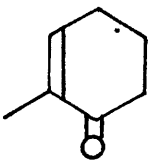
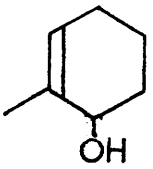


Mechanism B



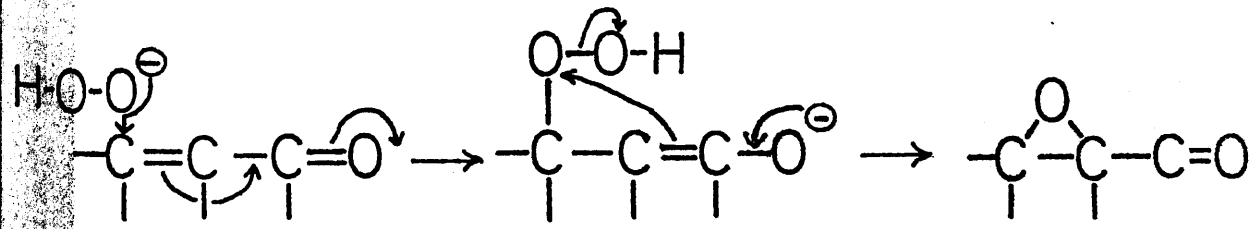
Mechanism C



				
TABLE 5 U.V. SPECTRUM				
$\lambda_{max.}$	238	-	235	-
ε	5630	-	10,000*	-
TABLE 6 N.M.R. SPECTRUM				
$\delta_{calc.}$	6.47	5.59	6.54	5.66
$\delta_{obs.}$	6.16	5.60	6.66	5.56
$\Delta\delta_{obs.}$	0.56		1.10	

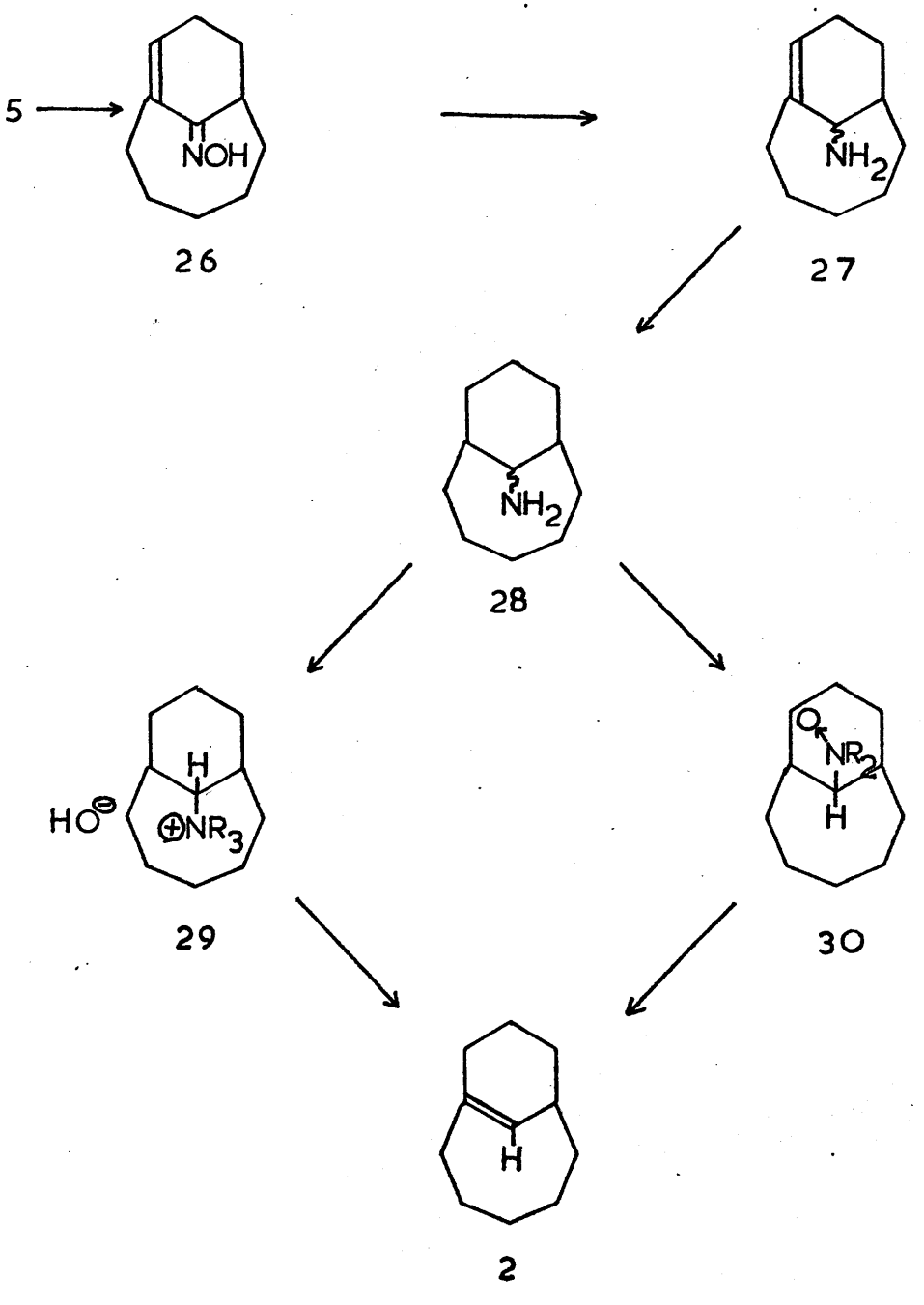
* Average value taken from References 52,53,54.

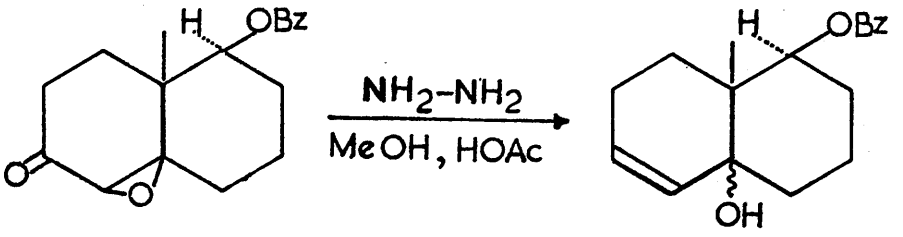
SCHEME 4



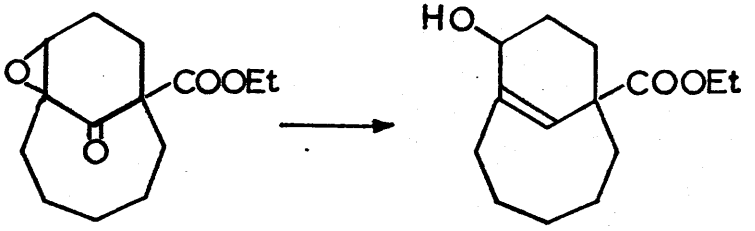
(i) (ii)

SCHEME 5





31 32



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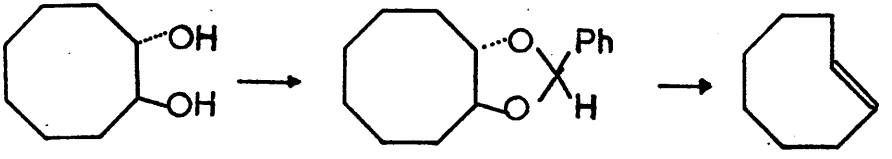

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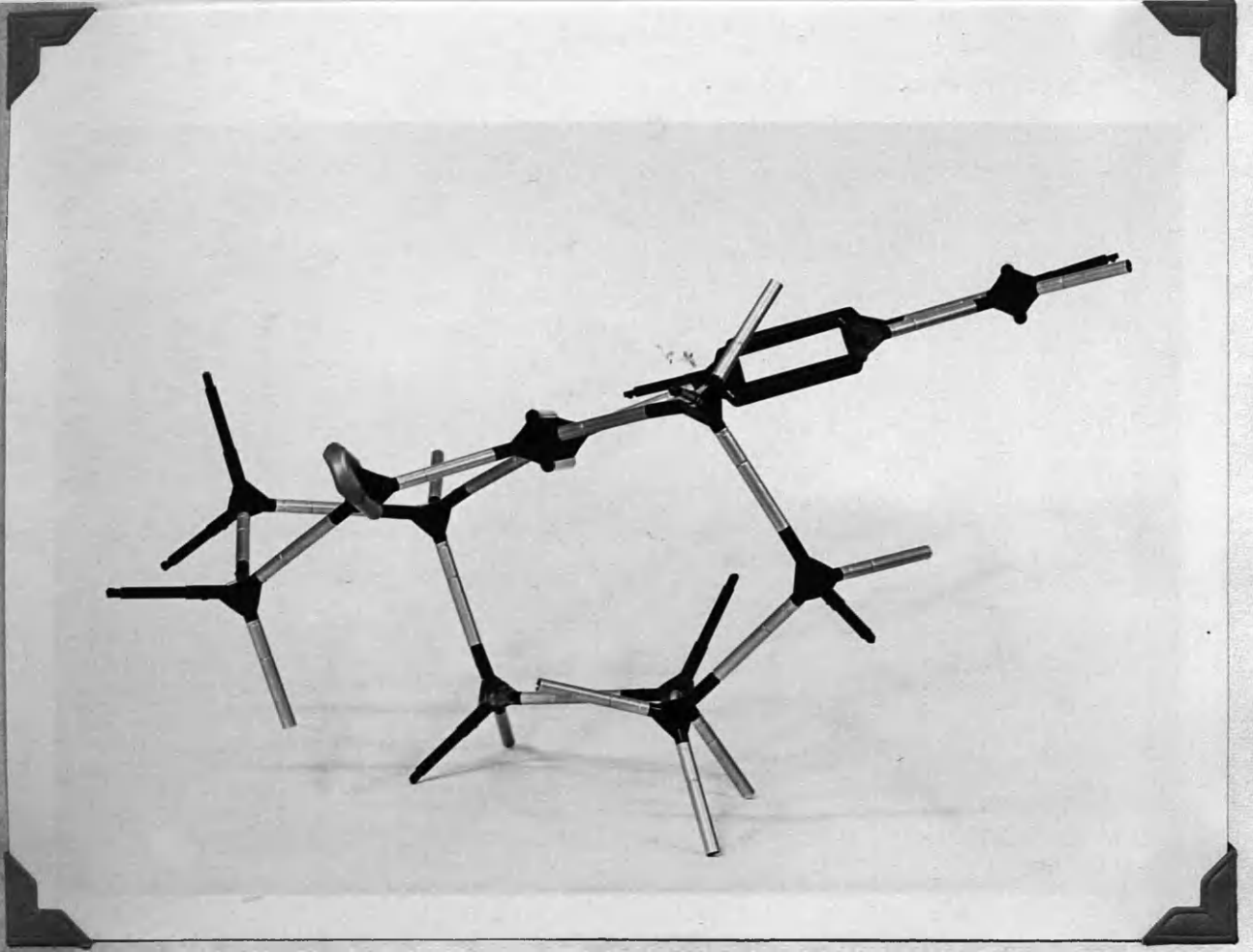
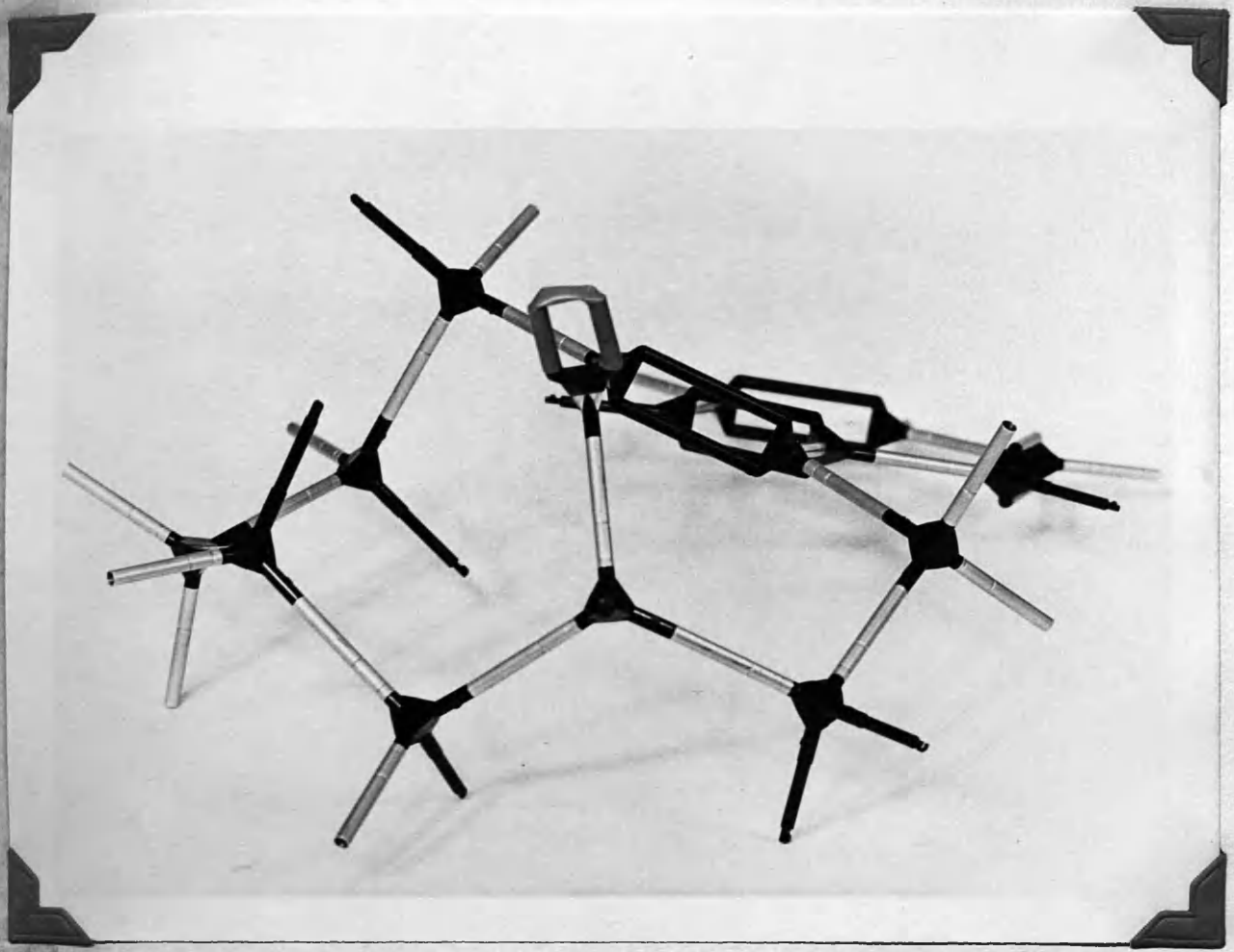


11-PHENYL BICYCLO(5.3.1.)UNDEC-7(11)-ENE-8-ONE

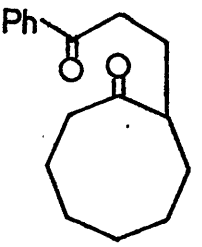
Shown along the twisted 7,11 bond



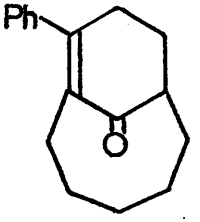
8-PHENYL BICYCLO(5.3.1.)UNDEC-7-ENE-11-ONE

Shown along the 7,11 bond

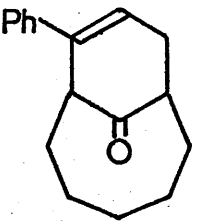
SCHEME 6



37



38



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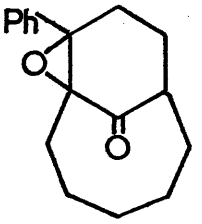

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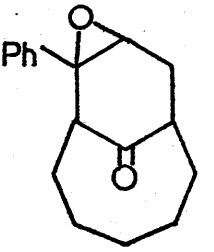

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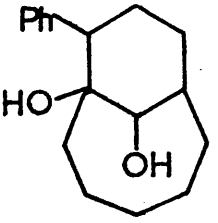

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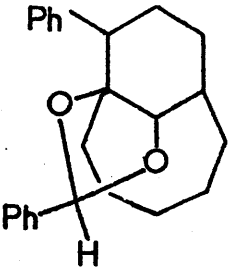

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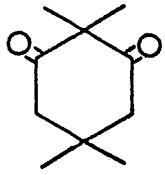
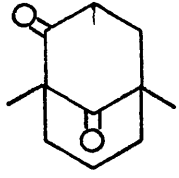
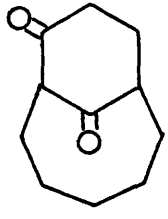
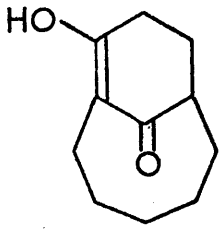
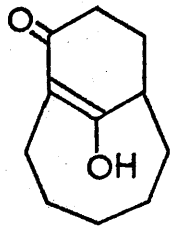
TABLE 7

COMPOUND	SOLVENT	ν_1	ε_1	ν_2	ε_2	$\nu_1-\nu_2$	$\varepsilon_2/\varepsilon_1$	REFERENCE
	Hexane	1736	368	1705	817	31	2.2	31
	CCl_4	1734	394	1700	980	34	2.5	
	$CHCl_3$	1730	364	1694	930	36	2.6	
	CH_3CN	1730	357	1695	945	35	2.6	
	Hexane	1741	245	1712	735	29	3.0	55
	CCl_4	1737	230	1707	730	30	3.2	
	$CHCl_3$	1729	255	1701	725	28	2.8	
	CH_3CN	1728	250	1702	646	26	2.5	
	Hexane	1732	165	1708	392	24	2.4	
	CCl_4	1729	203	1704	475	25	2.3	
	$CHCl_3$	1725	230	1698	364	27	1.6	
	CH_3CN	1725	185	1698	285	27	1.5	



44



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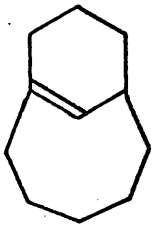

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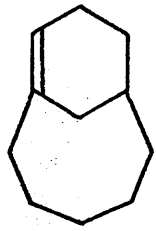

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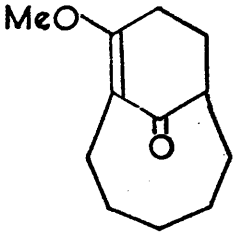

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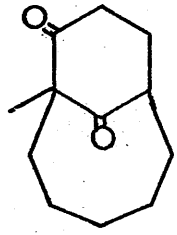

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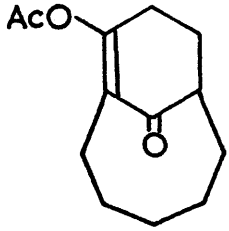

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SCHEME 7

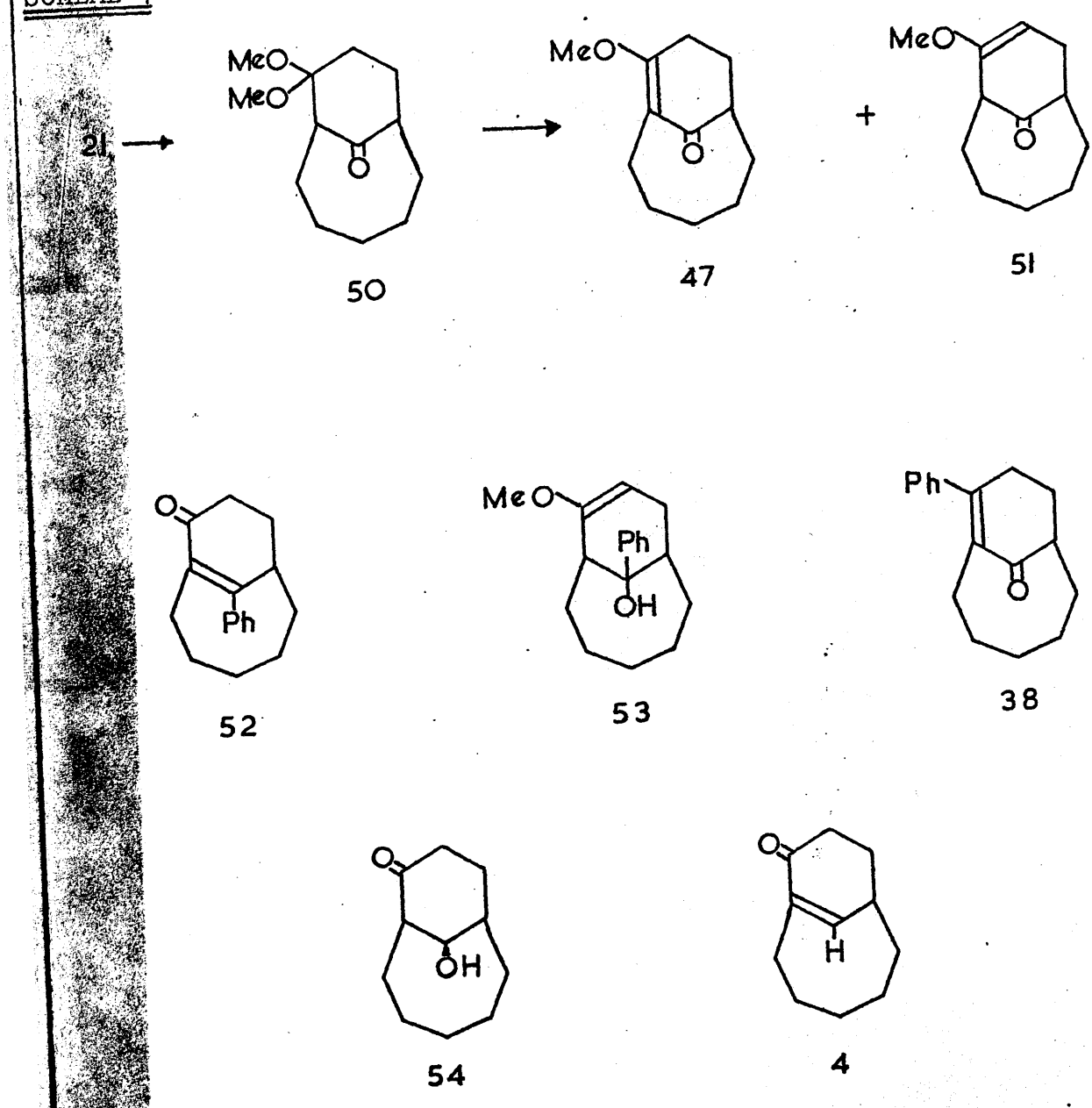


TABLE 8

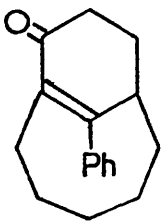
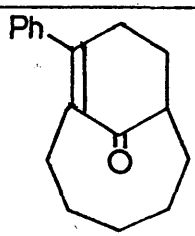
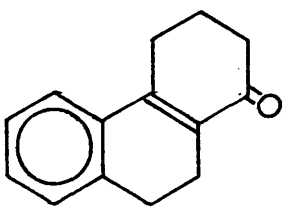
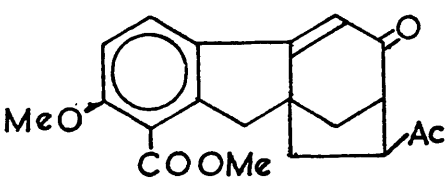
COMPOUND	$\lambda_{max.}^{EtOH}$ (E.T.)	ε	REFERENCE
	309	13,500	
	263	12,200	31
	300 320	16,000 15,000	56
	308 340	12,300 21,800	57

TABLE 9

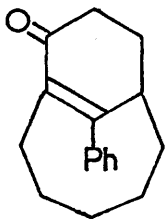
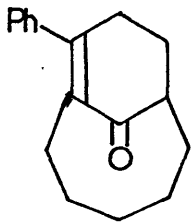
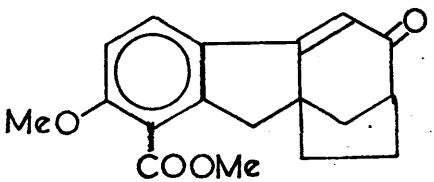
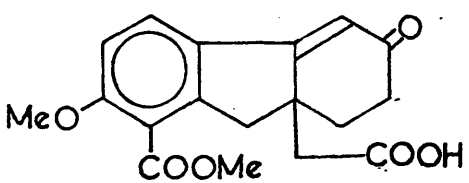
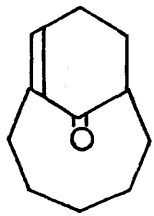
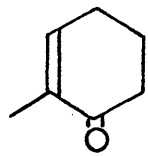
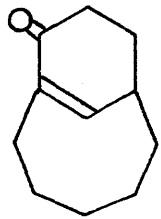
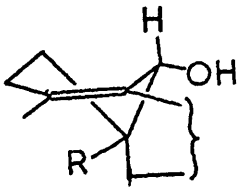
COMPOUND	$\nu_{C=O}^{CCl_4}$	$\nu_{C=C}^{CCl_4}$	REFERENCE
	1655	1649	
	1693	(1683)sh.	31
	1655	1620	57
	1654	1618	57

TABLE 10

			
I.R. $\nu_{C=O}$	$1702cm^{-1}$	$1670cm^{-1}$ Reference 51	$1675cm^{-1}$
N.M.R. $\delta, \beta H$	6.15δ	6.66δ	6.85δ
U.V. $\lambda_{max.}$	238nm.	235nm.	254nm.
ε	5630	10,000*	7,500
G.L.C. R_I (5% Q.F.1)	1870	-	1888

* Average value taken from References 52,53,54.



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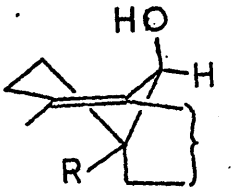

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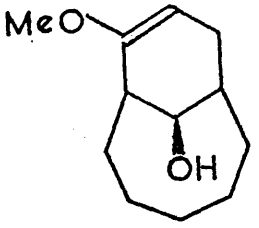

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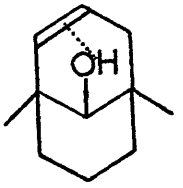

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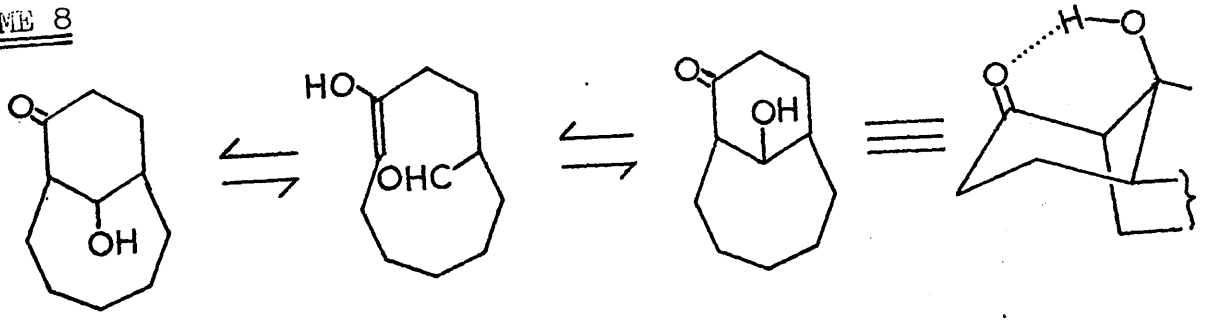
EME 8



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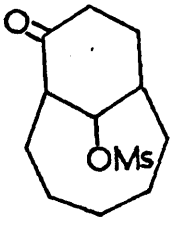

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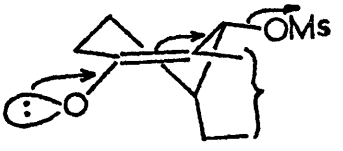

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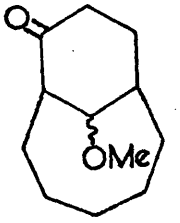

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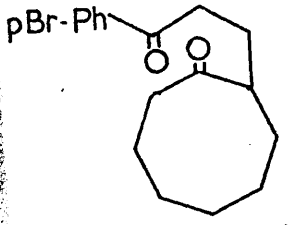

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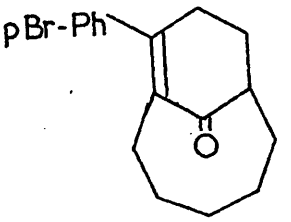

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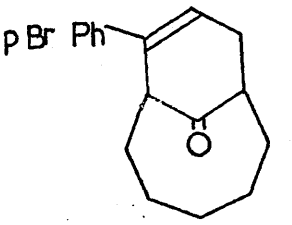

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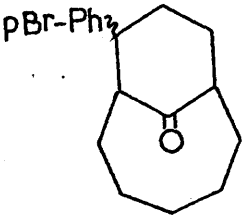

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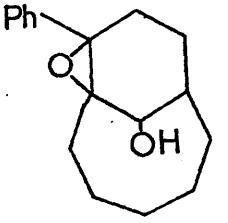

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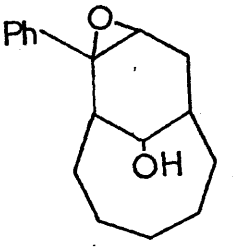

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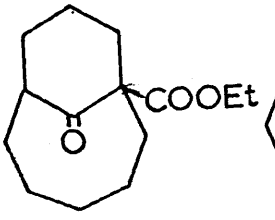

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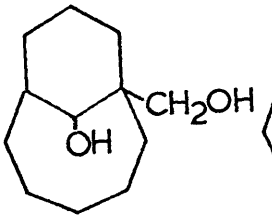

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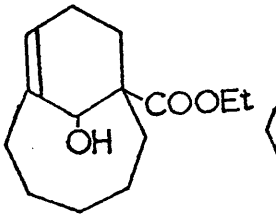

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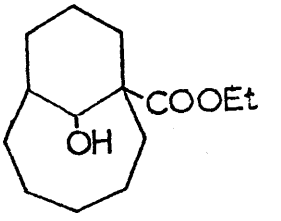

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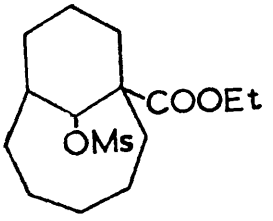

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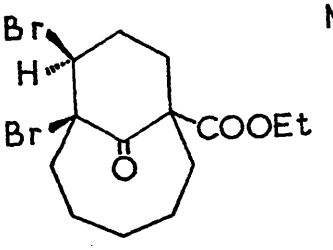

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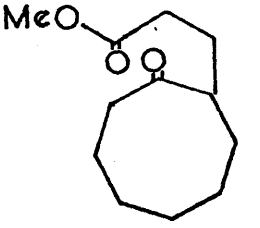
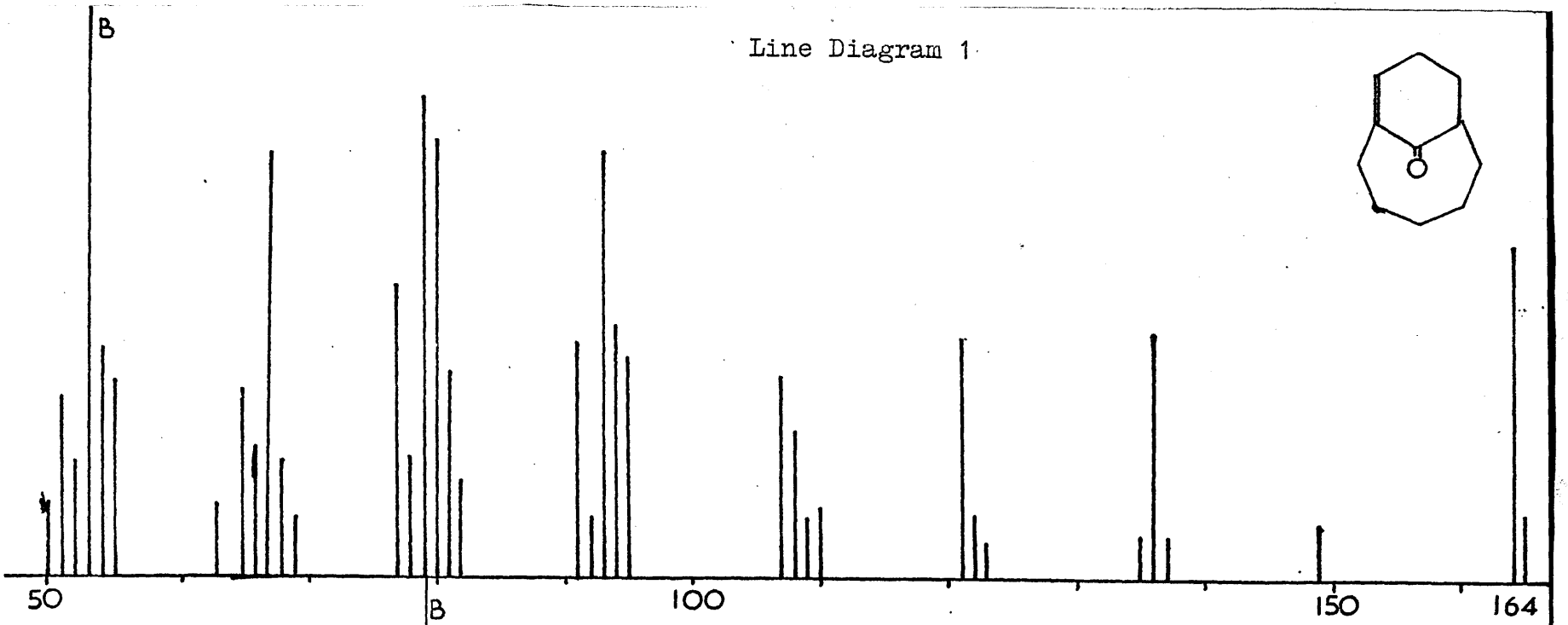
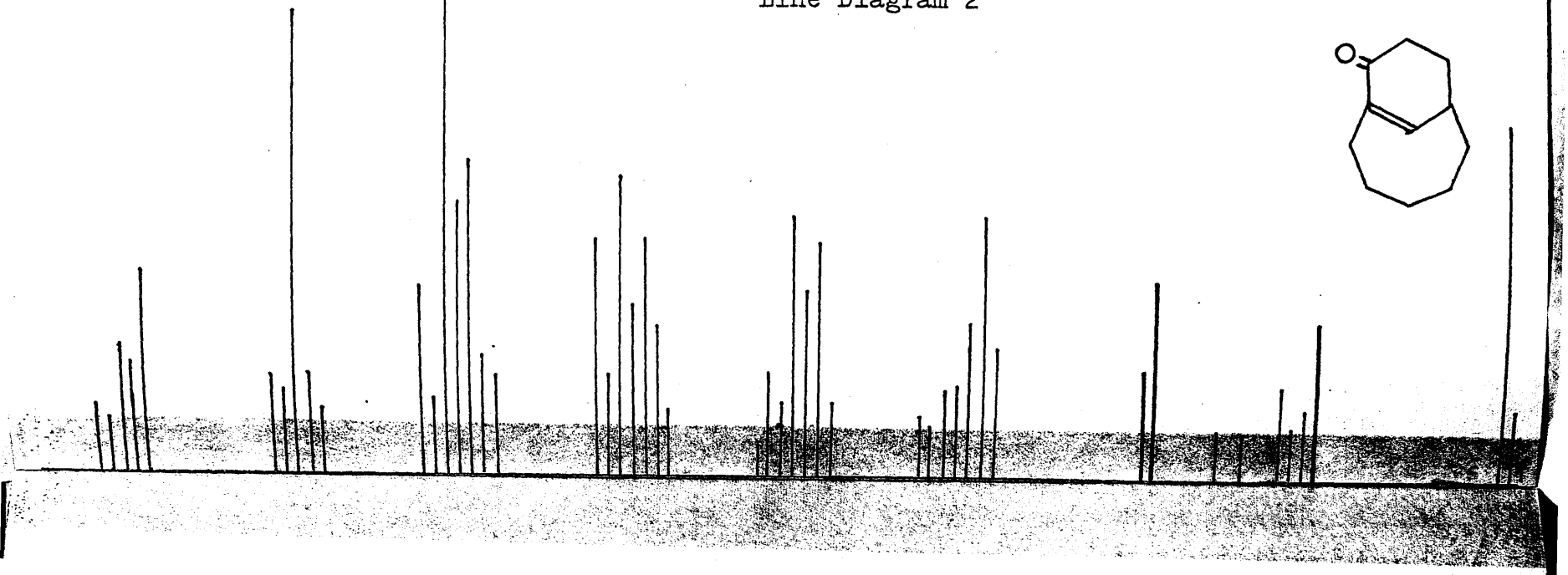


74

Line Diagram 1



Line Diagram 2



E X P E R I M E N T A L

All melting points were determined on a Kofler hot stage microscope and are uncorrected. Routine infra-red spectra of liquid films and nujol mulls were recorded on a Unicam SP200 spectro-photometer and quantitative infra-red absorption spectra on a Perkin Elmer grating infra-red spectro-photometer, Model 225.

Ultra-violet absorption spectra, measured on a Unicam SP800 spectro-photometer, refer to solutions in ethanol, unless otherwise stated.

Nuclear magnetic resonance spectra were obtained on the Perkin Elmer R10 and laterly on the Varian T60 spectro-photometers using ca. 0.3 molar solutions of deuterochloroform, unless otherwise indicated, with tetramethyl silane as internal standard.

Gas-liquid chromatography was carried out on Pye Argon and Perkin Elmer F11 gas chromatographs.

Chromatoplates, both for analytical and preparative use were made by the method of Stahl using Kieselgel G (Merck).

High resolution mass spectra were recorded on the A.E.I. MS12 mass spectrometer.

Work Up Procedures

METHOD A

The reaction mixture was extracted with the specified solvent and the organic extracts were washed with saturated aqueous sodium bicarbonate solution and saturated brine, before drying over anhydrous magnesium sulphate. The drying agent was removed by gravity filtration and the solvent was removed under reduced pressure on a 'Buchi Rovap'.

METHOD B

The residue was extracted with the specified solvent, washed with saturated brine and dried over anhydrous magnesium sulphate. The drying agent and solvent were removed as in (A) above.

3-(N,N DIMETHYLAMINO) - PROPIOPHENONE HYDROCHLORIDE

This Mannich base was prepared in 85% yield as its hydrochloride by the method of Org. Rns. Coll. Vol.III, p.305.

2-(3'-PHENYL - 3'-OXOPROPYL) -CYCLOOCTANONE (37)

To the Mannich base hydrochloride, (20g, 0.09 mole) dissolved in warm water was added, dropwise, with stirring 4 N sodium hydroxide solution until no further turbidity was observed. The mixture was cooled and treated with ether as in work-up B, using a water bath kept below 50°C for solvent removal, to yield 15.2g (83%) of the free Mannich base.

14.8g (0.08 mole) of the free Mannich base and 29.8g (0.24 mole) of cyclooctanone were refluxed under an air condenser for 40 minutes, steps being taken for removal of the evolved dimethylamine gas. The reaction mixture was neutralised by addition of glacial acetic acid and treated as in work-up A, using ether as solvent. Distillation of the residue gave unchanged starting ketone, together with (37), $b_{0.3}$ 170 - 172° i.r., ν max 1692 and 1700 cm^{-1} and, in a nujol mull spectrum 690 and 750cm^{-1}. The u.v. had benzenoid bands at 208 and 280 nm. and an E.T. band at 242 nm.

8-PHENYL-BICYCLO (5.3.1) UNDEC-7-ENE-11-ONE (38) and 8-PHENYL-BICYCLO (5.3.1) UNDEC-8-ENE-11-ONE (39)

Method a)

The diketone (37)(1.3g), 10 ml. of glacial acetic acid and 2 ml. of c. HCl were refluxed together for 18 hours. The bulk of the acetic acid was removed under reduced pressure and the residue diluted with water before work-up A, using benzene as solvent. Distillation of the residue gave a clear, viscous, yellow oil $b_{0.3}$ 150 - 160° which was shown by g.l.c. to contain two compounds, together with traces of starting diketone.

Extensive column and preparative thin layer chromatography failed to produce either of the two compounds in a pure state. It was concluded that these compounds were equilibrating on attempted separation. U.v. spectra of mixtures enriched in the major isomer, which made up 70% of the total, showed λmax 243 n.m., and enriched in the minor isomer (30%) showed λmax 263 nm.

Method b)

Paratoluene sulphonic acid (2.0g) in benzene (50 ml) was refluxed in a Dean and Stark water separator for 1 hour before addition of (37) (2.5g). This mixture was refluxed for 8 hours, neutralised by addition of anhydrous potassium carbonate and left standing overnight. The solution was

filtered and the benzene filtrate subjected to work-up B, to give a brown oil, which on reduced pressure distillation gave 1.49g (64%) of a pale yellow oil $b_{0.3}$ 150 - 158°, shown by g.l.c. to be identical with the major isomer above and to contain less than 1% of the minor isomer found above. The product from this cyclisation was therefore formulated as (39) and was identical to the compound obtained by A.M Lawson[31].

4 BROMO-ω-(N,N DIMETHYLAMINO) - PROPIONOPHENONE HYDROCHLORIDE

This Mannich base was prepared as its hydrochloride by the method of Knott[38].

2-(3'-p BROMOPHENYL, 3' OXOPROPYL) - CYCLOOCTANONE (62)

The Mannich base (49.0g) was liberated from its hydrochloride and refluxed with cyclooctanone (72.0g) as above. Work-up B followed by crystallisation of the product from 40 - 60 petrol yielded 41.7g (65%) of (62), m.pt 65-6. (Found: C,70.8; H, 8.8. $C_{17}H_{21}O_2Br$ requires C, 60.52; H, 6.28%). The ultra-violet spectrum showed an E.T. band at 256 nm (ε = 3,920). The infra-red spectrum (nujol mull) showed a broad carbonyl band centred on 1700 cm^{-1}. The n.m.r. spectrum showed for the aromatic protons at 2.4τ(4H) a typical $A'_2B'_2$ pattern; for the protons α to carbonyl functions an envelope between 7.0 and 7.8τ(5H) and

an envelope for the ring and chain methylene groups, at 7.8 to 8.6τ(12H). G.L.C. retention time on 4' of 1% QF1 (gas flow 50 ml/min) at 170° was 39 minutes.

8-(p BROMOPHENYL)- BICYCLO (5.3.1) UNDEC-8-ENE-11-ONE (64)

Cyclisation of (62) (34g) using the benzene/sulphonic acid method described for the nor-bromo compound, yielded 19.6g (60%) of (64) obtained by crystallisation, from 40 - 60 petrol, of the distillate b_{3mm} 140 - 160°C. Under conditions identical to those used to characterise the diketone (62) the bicyclic ketone (64) had relention time 19 minutes. The product had m.pt 93 - 4°C (40-60 petrol). (Found: C, 64.15; H, 6.06. $C_{17}H_{19}O$ Br requires C,63.96; H, 6.00%). The compound showed λmax 222nm (ε = 9,450) and 249 nm (ε = 16,000) in the uv and in the i.r. showed νC = O 1695cm^{-1}. The n.m.r. spectrum again showed a typical $A'_2B'_2$ system centred on 2.7τ (4H) for the aromatic protons, a broad singlet ($W_{\frac{1}{2}}$ = 8Hz) centred on 4.0τ (1H) due to the vinylic hudrogen, at 6.65τ (1H) a triplet (J = 6Hz) due to the C - 7 proton, and a multiplet (3H) between 7.3 and 7.7τ, as well as the methylene envelope (10H) resonating between 7.8 and 8.8τ.

8- (p BROMOPHENYL)- BICYCLO (5.3.1) UNDEC-8-ENE-11 OL

The ketone (64) (282 mg, 0.89 m.mole), was stirred at room temperature with lithium aluminium hydride (66.5 mg 1.75 m.mole) in ether (25 ml.), for 30 minutes. Excess hydride was destroyed with a saturated aqueous solution of sodium sulphate. The reaction was worked up by method B to yield 201 mg of material, which was shown by T.L.C. to contain some starting ketone. The product was isolated by prep. TLC and showed λmax 248 nm. ν_{OH} 3618 cm^{-1} (secondary hydroxyl).

ISOMERISATION OF (39)

1. ACETIC ACID - TRIETHYLAMINE

8 - (p Bromophenyl) - bicyclo (5.3.1) undec - 8 - ene - 11 - one (300 mg.) was refluxed in a mixture of glacial acetic acid (3 ml) and triethylamine (20 ml) for 24 hours, under an atmosphere of nitrogen. The cooled reaction mixture was neutralised with 6N HCl, poured into water and worked up by method B using ether as extractant. Solvent removal gave 283 mg of unchanged starting material (t.l.c./g.l.c./i.r.)

2. HYDROCHLORIC ACID - ACETIC ACID

The unconjugated bicyclic enone (64) (180 mg) was refluxed in a mixture of glacial acetic acid (5 ml) and c. HCl (1 ml) under a nitrogen atmosphere for 24 hours. Most of the acetic acid was removed under

reduced pressure and the residue was flooded with water. Work-up method A (benzene) yielded 168 mg of material, shown by g.l.c. to consist of two compounds in the ratio 80:20, of which the major isomer had retention time identical to (39).

A repeat of this procedure on 1.63g of bicyclic ketone (64), when 1.59g of material was recovered gave approximately the same product composition (78:22).

8 - (p-BROMOPHENYL) - BICYCLO (5.3.1) UNDECAN-11-ONES (65)

1. 10% Palladium on Carbon - Ethyl Acetate - 1 Atmosphere

The unsaturated bicyclic ketone (64) (150 mg) was dissolved in ethyl acetate (10 ml) containing 250 mg of 10% palladium on carbon powder. This mixture was stirred at room temperature under an atmosphere of hydrogen for 20 minutes. The reaction mixture was filtered through celite and the solvent removed to yield 152 mg of material with t.l.c., g.l.c., and n.m.r. identical to starting material.

2. 30% Palladium on Carbon - Ethyl Acetate - 1 Atmosphere

Treatment as above of the enone (64), (438 mg), with 50 mg of 30% palladium on carbon powder for 1 hour again gave quantitative recovery of starting material (64).

3. 5% Palladium on Calcium Carbonate - Ethanol - 3 Atmospheres

175 mg of bicyclic ketone (64) was dissolved in ethanol (2 ml) containing 5% palladium on calcium carbonate (22 mg) and shaken for 3 hours under 3 atmospheres pressure of hydrogen. Work-up as above gave 175 mg residue which by g.l.c. analysis was composed mainly of (64) with its two dihidroderivatives present to the extent of ca 1%.

4. 10% Palladium on Barium Sulphate - Acetic Acid - 6 Atmospheres

The bicyclic ketone (6.4) (8.0g) was dissolved in acetic acid (34 ml) containing 3 g of 10% palladium on barium sulphate and the mixture shaken under a pressure of 6 atmospheres of hydrogen for 4 hours. Removal of most of the solvent under reduced pressure followed by work-up A (ether) yielded 6.7g residue shown by g.l.c. analysis to consist of 91% of (64), together with 9% of the two dihydro compounds (65) epimeric at C - 8. These two product peaks had R_t 14.4 and 15.6 mins on a 4' column of 5% QF1 at 150° (gas flow rate 50 ml/min.) Under these same conditions (64) has R_t 55 mins.

ATTEMPTED PREFERENTIAL EPOXIDATION OF αβ ENONE (38)

A mixture of the enones (38) and (39) in the ratio 4:1 (850 mg) was dissolved in ethanol (6 ml) and this solution added to a solution of 8% sodium hydroxide (1.2 ml) and 15% hydrogen peroxide (1.2 ml). The mixture was warmed on a steam bath for two minutes and allowed to stand at room temperature for 24 hours. The reaction mixture was poured into water and extracted with ether, followed by work-up B to yield 725 mg of material having the same t.l.c. and i.r. as starting mixture. G.l.c. showed no change in the relative intensities of the peaks due to (38) and (39).

ATTEMPTED PREFERENTIAL EPOXIDATION OF βɣ ENONE (39)

A mixture of enones (38) and (39) in the ratio 4:1 (14.5g 0.06 mole) was dissolved in 75 ml of analar chloroform and added to a solution of (12.0g 0.075 mole) of metachloroperbenzoic acid in 100 ml[1] analar[1] chloroform. The mixture was allowed to stand in the dark for 5 days. After filtration, to remove precipitated acid, the organic layer was washed with 10% sodium besulphite to destroy excess paracid, then successively with saturated sodium carbonate and saturated brine before drying over magnesium sulphate. Solvent removal gave 13.2 g residue, a t.l.c. of which showed two spots Rf 0.4 and 0.3 in 15% ethylacetate petrol.

Crystallisation of the reaction residues from ethyl-

acetate yielded the compound of Rf 0.3 free of the other compound. This compound had the following characteristics m.pt. 124 - 5°C (EtoAc). (Found: C, 79.49; H 7.91. $C_{17}H_{20}O_2$ requires C, 79.65; H 7.86%) The i.r. spectrum showed νC = O 1712 cm^{-1} and ν O H 2980 cm^{-1}. The n.m.r. spectrum showed a sharp singlet at 2.62τ (5H) for the aromatic protons, a broad singlet ($W_{\frac{1}{2}}$ = 5 Hz) at 6.32τ (1H) due to the epoxide ring (C - 9) hydrogen, a multiplet centred on 6.9τ (1H) due to the C - 7 proton and a broad singlet ($W_{\frac{1}{2}}$ = 4Hz) at 7.45τ (2H), as well as the methylene envelope between 7.8 and 8.7τ (11H). This data is consistant with 8α - phenyl - 8β, 9β-epoxy, bicyclo (5.3.1) undecan-11-one (41).

The minor product (Rf = 0.4) from this reaction was obtained by chromatography, on silica gel, of the mother liquor, after removal of most of (9). It was recrystallised from ethyl acetate to m.pt 50 - 51° to give the data presented here. (Found: C, 79.35; H, 7.68. $C_{17}H_{20}O_2$ requires C, 79.65; H, 7.86%) The i.r. spectrum showed ν C = O 1728 cm^{-1}. The n.m.r. spectrum showed a multiplet centred on 2.6τ (5H) due to the aromatic protons. The remainder of the protons (15H) resonated as a broad envelope between 7.2 and 9.2τ. This data is consistant with 8α-phenyl-7β,8β-epoxy, bicyclo (5.3.1) undecan-11-one (40).

8 α - Phenyl, - 7β,8β-epoxy - bicyclo (5. 3.1) undecan - 11 ol (66) and 8α Phenyl, - 8β,9β epoxy - bicyclo (5.3.1) undecan - 11 ol (67)

A mixture of the epoxy ketones (40) and (41) (10.15g, 0.04 moles) was added as a solution in anhydrous ether (25 ml), drop wise, with stirring to a suspension of lithium aluminium hydride (3.75g, 0.10 moles) in anhydrous ether (25 ml) and the mixture was stirred at room temperature for 24 hours. Excess hydride was destroyed by careful addition of a saturated solution of sodium sulphate (5 ml). The reaction mixture was filtered, washed with saturated brine and dried over magnesium sulphate. Solvent removal yielded 10.7g of residue as a white crystalline mass, the i.r. of which showed no ν c = o. T.L.C. revealed two spots, the major of which was obtained free of the minor, by careful crystallisation from diethyl ether, and had the following properties : m.pt. 106.5 - 108 (Diethyl ether) (Found: C, 78.98; H, 8.53. $C_{17}H_{22}O_2$ requires C, 79.03; H, 8.58%). The mass spectrum showed a molecular ion at 258. The i.r. showed νOH 3620cm^{-1} (ε_a = 14), bands at 1053 and 1069 cm^{-1} in the fingerprint region, and ν O H 2980 cm^{-1}. The n.m.r. spectrum showed at 2.60τ (5H) a sharp singlet for the aromatic protons, at 5.50τ (1H) a broad singlet ($W_{\frac{1}{2}}$ = 4 H_z) for the carbinyl proton, and at 6.42τ (1H) a doublet (J = 4H_z) due to the epoxide proton (C - 9). When hexaduetero-

dimethyl sulphoxide was added the spectrum changed to show, at 5.42 τ (1H) a doublet (J = 5Hz) for the carbinol proton, at 5.75 τ (1H) a broad singlet ($W_{\frac{1}{2}}$ = 12Hz) due to the carbinyl proton, and the epoxide proton resonance at 6.45 τ (1H), a doublet (J = 4Hz). This data is consistant with 8α - phenyl, - 8β,9β-epoxy, bicyclo (5.3.1) undecan-11-ol (67).

The minor product was obtained by column chromatography, on silica, of the mother liquors after crystallisation of (12) and had m.p 92-92.5°(60 - 80 petrol). (Found: C, 79.14; H, 8.53. $C_{17}H_{22}O_2$ requires C, 79.03; H, 8.58%). Molecular Weight 258 (Mass Spectrum). The i.r. showed νOH 3623 cm^{-1} (ε_a = 11) and bands at 1040 and 1075 cm^{-1} in the fingerprint region. The n.m.r. spectrum showed, at 2.60 τ (5H) a broad multiplet ($W_{\frac{1}{2}}$ = 12Hz) for the aromatic protons, at 6.05 τ (1H), a doublet (J = 6Hz) for the carbinyl proton, coupled to the C -1 bridgehead proton, and the methylene envelope between 7.4 and 9.4 τ (16H). On addition of hexadeutero-dimethyl sulphoxide, the spectrum showed a doublet (J = 4.5 Hz) at 4.70 τ (1H) due to the carbinol proton coupling to the carbinyl proton, and at 6.25 τ (1H) the signal for the carbinyl proton appeared as a skewed triplet.

This data is consistant with structure (66).

8α Phenyl, bicyclo (5.3.1) undecan - 7, 11 - diol (42)

The epoxy alcohol (66) (100 mg) was dissolved in ethanol (20 ml) containing 10% palladium on carbon (50 mg). The mixture was stirred in an atmosphere of hydrogen, until hydrogen uptake was 19 cc (Theoretical = 9.5 cc) when the catalyst was removed by filtration through celite. Solvent removal yielded 93 mg of material which by t.l.c. was seen to contain 40% starting material. Separation of a sample was achieved by preparative t.l.c. to give 16 mg of diol (42). The i.r. spectrum showed ν OH 3585 and 3558 cm^{-1}. The n.m.r. spectrum showed, at 2.72 τ (5H) a sharp singlet due to the aromatic hydrogens, at 5.30 τ (1H) a triplet (J = 7Hz) at 5.95 τ (1H) a quartet (J = 4 Hz), at 7.0 τ (1H), a quartet (J = 4Hz) and the methylene envelope at 7.3 to 8.9 τ (16H). The spectrum when hexa-deuterodimethyl sulphoxide was added to the solution failed to show any signal assignable to the secondary hydroxyl function at C - 11, but did show a sharp singlet at 6.28 τ due to a tertiary hydroxyl. The compound obtained from the above reaction, formulated as (42), had a g.l.c. retention time of 15.5 minutes on a 4' column of 5% QF1 at a temperature of 175°C (gas flow rate 46 ml/min)

Attempted Preparation of the O - O - Benzylidene Acetal of (42)

Attempted preparation of the O-O-Benzylidene Acetal

(43) of diol (42).

The diol (42) (14 mg), anhydrous benzene (2 ml) and benzaldehyde (1 ml) were refluxed overnight in the presence of toluene-p-sulphonic acid (1 mg), under a Dean and Stark water separator, in an atmosphere of nitrogen. Work up procedure B using benzene as extractant yielded 12 mg of brown viscous syrup shown by t.l.c. analysis to contain not less than 10 compounds.

1- PYRROLIDINOCYCLOOCTENE

This enamine, $b_{0.2}$ 90 - 92° was prepared in 68% yield by the method of Kuehne[8], except that toluene was used as azeotrope.

1- MORPHOLINOCYCLOOCTENE

Attempted preparation of the morpholine enamine of cyclooctanone by the method used by Stork and Landesman[9] to prepare 1 morpholino cycloheptene, yielded only 39% of 1 morpholinocyclooctene.

2- CARBETHOXY-CYCLOOCTANONE

1. PYRROLIDINE ENAMINE ACYLATION

Acylation of 1-pyrrolidino cyclooctene with ethyl chloroformate by the general method of Stork[43] yielded only 8% of the desired ketoester.

2. MORPHOLINE ENAMINE ACYLATION

Acylation of 1 morpholinocyclooctene with ethyl chloroformate by the general method of Stork[43] yielded only 7% of the desired keto-ester.

3. SODIUM HYDRIDE - DIETHYL CARBONATE

The keto-ester was prepared in 80% yield by the method of Rhoads[39].

MICHAEL ADDUCT OF ACROLEIN WITH 2 CARBETHOXY CYCLOOCT.

1. TRIETHYLAMINE

The method of Buchanan and McLay[40] yielded only 38 mg of the desired 2 - ethoxycarbonyl - 2 - (3' oxopropyl)-cyclooctanone[6] from 1.56 g of 2 carbethoxy cyclooctanone.

2. SODIUM ETHOXIDE

The method of Warnhoff[4] was used to prepare 2 - ethoxycarbonyl - 2 - (3' oxopropyl) - cyclooctanone (6) in 64% yield.

CYCLISATION OF 2 - ETHOXY CARBONYL - 2 - (3' OXOPROPYL)-CYCLOOCTANONE

1. BENZENE - p TOLUENE SULPHONIC ACID

4.7g of Michael adduct (6) was dissolved in benzene (20 ml) and added to 20 ml of benzene containing paratoluene sulphonic acid (1g). The mixture was refluxed for 18 hours in a Dean and Stark water

separator, under a nitrogen atmosphere. The solution was neutralised by standing at room temperature overnight over potassium carbonate, filtered, and dried over magnesium sulphate. Solvent removal left 3.35g of residue, which by fractional distillation under reduced pressure gave several products, none of which had the properties of the desired product.

2. N,N,N - TRIMETHY-N-BENZYL AMMONIUM HYDROXIDE ('TRITON B')

A mixture containing the michael adduct (6) (24.5g), 10 ml of a 40% (W/W) solution of 'Triton B' in methanol, and methanol (10 ml) was refluxed for 5 hours. After cooling the reaction mixture was poured into a sodium chloride/ice mixture and the organic compounds extracted into ether. The ethereal layer, after washing with 1N sulphuric acid, saturated brine, drying over magnesium sulphate yielded on solvent removal 17.3g of residue which showed intense OH absorption and very little of the aldehydic hydrogen stretch present in the infra-red spectrum of (6). Fractional distillation under reduced pressure gave fractions which were shown by t.l.c./i.r. analysis to consist of aldol product (7) and Michael adduct (6) in a constant ratio. It was assumed that (6) arose from occurrence of the retro-aldol reaction of (7) during distillation.

ATTEMPTED DEHYDRATION OF (7)

1. Anhydrous Oxalic Acid

A mixture of ethyl-8-hydroxy, bicyclo-(5.3.1)-undecan-11-one carboxylates (7) (110 mg) and anhydrous oxalic acid (59 mg) was heated on an oil bath at 210° for 40 minutes. The ether extracts of the cooled reaction mixture were worked-up by method A, to yield 39 mg of residue with t.l.c. and i.r. identical to starting material.

2. Oxalic Acid - Triethyl Amine

A mixture of ethyl-8-hydroxy, bicyclo-(5.3.1)-undecan-11-one carboxylates (7) (1.24 g), triethylamine (4.4 ml) and anhydrous oxalic acid (0.62 g) was refluxed in a nitrogen atmosphere for 87 hours. The cooled reaction mixture was diluted with ether, the etheral extracts being washed with 1$\bar{N}$ sulphuric acid, saturated sodium bicarbonate and saturated brine. Solvent removal after drying over magnesium sulphate gave 1.01 gm of residue. T.L.C. and i.r. analysis showed only very slight differences from starting material, but an n.m.r. spectrum of the crude product showed traces of vinylic hydrogen absorption at 3.8τ.

3. Oxalic Acid - N,N (Di-n-Butyl) Amine

The aldol (7) (1.63 g), oxalic acid (0.82 g) and di(n)butylamine (7.4 ml) were refluxed under nitrogen for 43.5 hours. Work up as above gave 1.08 g residue which had t.l.c., i.r. and n.m.r. very similar to that found above.

4. Oxalic Acid - Tri (n Butyl) Amine

The aldol (7) (3.5 g), oxalic acid (1.75 g) and dri-n-butylamine (17.5 ml) were refluxed under a nitrogen atmosphere for 60 hours. Work-up as above gave 1.1 gm residue which was shown by t.l.c. comparison with a known sample to contain ca 10% of the required dehydration products (8) and (9).

CYCLISATION AND DEHYDRATION OF MICHAEL ADDUCT (6)

The Michael adduct (6) was cyclised and dehydrated by the method of Warnhoff et al[4] in 75% yield. Recrystallisation of the major product, ethyl, 11-oxobicyclo (5.3.1) undec-7-ene-1-carboxylate[8] from 40-60 petrol gave a white solid mp 53 - 4° with all the characteristics ascribed to it in the reference cited above. In addition, the compound gave 1 peak (R_t 16.6 min) on a 4 foot column of 5% QFI at a temperature of 150° and a gas flow rate of 50 ml/min, when subjected to g.l.c. analysis.

ETHYL, 11-OXOBICYCLO (5.3.1) UNDECAN - 1-CARBOXYLATE (63)

The bicyclo αβ enone ester (8) (418 mg) was dissolved in ethyl acetate (10 ml) containing 300 mg of 10% palladium on carbon powder and stirred in an atmosphere of hydrogen for 15 minutes. The solution absorbed 59 cc of hydrogen (theoretical 40 cc). Filtration of the solution through celite and solvent removal left 376 mg (89%) of (19) which showed no trace of starting material (u.v./n.m.r./g.l.c.) and which had all the properties ascribed to it[4]. In addition, under the g.l.c. conditions used for characterisation of (8), the keto-ester (68) had a retention time of 14 mins.

INADVERTANT PREPARATION OF 1 - (11-HYDROXYBICYCLO (5.3.1) UNDECANYL)-METHANOL (69)

The saturated keto ester (68) (500 mg 2.1 m mole), was dissolved in ethanol (5 ml) and added dropwise to a stirring suspension of sodium borohydride (0.38 g 1 m mole) in ethanol (5 ml). When addition was complete the reaction medium was stirred at room temperature for 60 hours. Excess borohydride was destroyed by addition of 2N̄ hydrochloric acid (1 ml). The reaction mixture was extracted with ether and worked up by method A. Solvent removal yielded 393.6 mg (98%) of a crystalline mass, which was shown by t.l.c. to be homogeneous. The crude product was recrystallised from

benzene to m.pt 123.5 to 124° and gave the following data: (Found: C: 72.84%, H: 11.13%, $C_{12}H_{22}O_2$ requires C: 72.68%, H: 11.18%.) The infra-red spectrum of this product, as a solution in CCl_4 showed ν_{OH} 3615 and 3540 cm^{-1} due to primary and secondary hydroxyl functions and further sharp absorptions at 1012, 1038 and 1065 cm^{-1}. The nuclear magnetic resonance spectrum showed a typical AB quartet[41] interpreted as being due to the methylene protons of the primary alcohol function whose rotation is restricted by intramolecular hydrogen bonding of the two hydroxyl functions. Application of the method described in Bible gives the weighted chemical shift of one of the protons as 6.48 and the other as 6.68 (J = 10 cps). The quartet integrates for 2 protons. A 1H doublet appears at 6.05 (J = 4 cps) due to the carbinyl hydrogen. The methylene envelope extends from 7.0 to 9.0τ and integrates for 19H. The mass spectrum showed a weak parent ion at 198, a medium intensity peak at 196 (M - 2H) and a strong peak at 180 (M - H_2O).

ETHYL, BICYCLO (5.3.1) UNDEC-7-ENE-11-OL CARBOXYLATE (70)

The enone ester (8) (2.2g., 9.45 m.mole) was dissolved in ethanol (10 ml) and added to a suspension of sodium borohydride (185 mg., 19.5 m.mole) in ethanol (15 ml). The reaction mixture was stirred at room temperature for 48 hours, when 1N hydrochloric acid (5 ml) was added to

destroy excess hydride. Ether was used as extractant in work up proceedure A, to yield 2.14g of residue. A sample of pure 70 was obtained by column chromatography of the crude product (2g) on grade 'O' alumina (60g). (Found: C, 70.56; H, 9.46. $C_{14}H_{22}O_3$ requires D, 70.56; H, 9.30%) The i.r. spectrum showed a sharp band at 3615cm^{-1} and a broad band between 3450 and 3600 cm^{-1}, with maximum height at 3540 cm^{-1}, attributable respectively to free and bonded hydroxyl functions. The carbonyl region showed a weak absorption at 1730 cm^{-1} and a strong absorption at 1706 cm^{-1}, attributable to free and hydrogen bonded ester groups. In the n.m.r. spectrum, the vinyl proton appeared at 4.41τ (1H) as a broad doublet (J = 3Hz) and the carbinyl proton at 5.52τ (1H) as a broad doublet (J = 6Hz). The ester group appeared at 5.82τ (2H) as a quartet (J = 8Hz) and at 8.74τ (3H) as a triplet (J = 8Hz). The carbinol protons gave rise to two signals, at 6.87τ (0.5H), a doublet (J = 4Hz) and at 6.22τ (0.5H), a doublet (J = 3Hz), both of which disappeared on addition of D_2O. The carbinyl proton signal, on addition of D_2O, collapsed to a broad singlet, losing its J = 6 coupling but still having a $W_{\frac{1}{2}}$ = 6Hz, probably due to allylic coupling with the vinylic hydrogen.

ETHYL BICYCLO (5.3.1) UNDECAN-11-OL CARBOXYLATE (71)

1. By Hydrogenation of 70

The allylic alcohol/ester 70 (300 mg) was dissolved in ethanol (10 ml) and added to a suspension of platinum oxide monohydrate (100 mg) in ethanol (15 ml). The solution was stirred in an atmosphere of hydrogen for 1 hour. Hydrogen uptake was 10 ml (theoretical 7.5 ml). After filtration through celite the solvent was removed under reduced pressure. Work up procedure B was then applied to yield 298 mg (98%) of product 71. (Found: C,70.16; H, 9.90. $C_{14}H_{24}O_3$ requires C, 66.96; H, 10.07%). The i.r. spectrum showed two carbonyl bands at 1730 and 1705 cm^{-1}, attributable to free and bonded ester functions respectively.

ETHYL - 7,8-EPOXYBICYCLO (5.3.1) UNDECAN-11-ONE CARBOXYLATE 33

A solution of the enone ester 8 (100 mg., 0.42 m.mole), and metachloroperbenzoic acid (100 mg., 0.5 m.mole) in chloroform (15 ml) was allowed to stand in a stoppered flask for 6 days. The organic solution was washed with saturated sodium sulphite, saturated sodium carbonate and saturated brine before drying over anhydrous magnesium sulphate. Solvent removal yielded 109.7 mg of material, shown by g.l.c. analysis to consist of 60% epoxide and 40% enone. A pure

sample of the epoxide (24) was obtained by preparative t.l.c. (Found: C,66.89; H, 8.03. $C_{14}H_{20}O_4$ requires C, 66.65; H, 7.99%). The infra-red spectrum shows ν (epoxide H) at 2970 cm^{-1}, ν (ester CH_2) 2855 cm^{-1} and two carbonyl bands, one due to the ester function at 1736 cm^{-1} and one due to the αβ epoxy carbonyl at the abnormally high $\nu_{c=o}$ 1724 cm^{-1}. The n.m.r. spectrum shows, at 5.8τ (2H) a quartet (J = 8Hz), due to the methylene group of the ester function; at 6.70τ (1H) a broad singlet ($W_{\frac{1}{2}}$ 4Hz) due to the epoxide hydrogen and at 6.70τ (3H) a triplet (J = 8Hz), due to the methyl of the ester function. The methylene envelope appeared between 7.3 and 9.0τ (14H).

ATTEMPTED PREPARATION OF ETHYL, BICYCLO (5.3.1) UNDEC-7(11)-ENE-8-OL CARBOXYLATE (34)

1. Hydrazine in Methanol

To the epoxy-keto-ester (33) (60 mg, 0.24 m.mole) dissolved in 5 ml of absolute methanol, was added, with stirring, at room temperature 32.5μl (0.60 m.mole) of 100% hydrazine hydrate. No evolution of nitrogen was observed and even after 1 hour at reflux the t.l.c. was unchanged.

2. Hydrazine in Methanol - Acetic Acid

To the epoxy ketone (33) (82 mg, 0.33 m.mole) in methanol (0.7 ml), at 0°C, was added with stirring 100% hydrazine hydrate (0.1 ml 1.0 m.mole) and glacial acetic acid (36µl, 0.06 m.mole). The reaction mixture was refluxed for 30 minutes and stirred at room temperature for 65 hours. Work up by method A gave 71 mg of material, the t.l.c. of which was identical to starting material.

1-ETHOXYCARBONYL, BICYCLO (5.3.1) UNDECAN-11-YL METHANE SULPHONATE (72)

A mixture of alcohol-ester 71 (105.5 mg, 0.44 m.mole), methane sulphonyl chloride (40 l, 0.50 m.mole-, and anhydrous pyridine (0.4 ml) was stored at 0°C for 24 hours. The reaction mixture was poured into 25g of ice containing 1 ml of 6N hydrochloric acid. The ice was allowed to melt and the aqueous phase was extracted with ether. The ethereal extracts were washed with 1N hydrochloric acid, saturated brine, saturated sodium bicarbonate, saturated brine and then dried over anhydrous magnesium sulphate. Solvent removal left 116 mg of residue. T.L.C. analysis (15% ethylacetate in 60 - 80 petrol) showed some starting material and 1 main product. Isolation of this product

by preparative t.l.c. gave 39 mg of an oil which could not be induced to crystallise and which decomposed on attempted distillation. The i.r. spectrum of this compound showed $\nu_{c=o}$ 1725 cm^{-1} and other absorptions at 1360, 1348, 1158, 950, 938, 910 and 873 cm^{-1}. The n.m.r. spectrum showed, at 4.7τ (1H) a doublet (J = 4.5Hz) due to the carbinyl hydrogen and at 7.1τ (3H) a singlet due to the methyl of the sulphonate ester as well as the usual ester quartet (J = 8Hz) at 5.92τ (2H) and ester triplet (J = 8Hz) at 8.79τ (3H). This data is consistant with formulation of the product as 72.

1 - (11-HYDROXY BICYCLO (5.3.1) UNDEC-7-ENYL) METHANOL (14)

The enone ester 8 (2.448g., 10.3 m.mole) dissolved in dry tetrahydrofuran was added to a suspension of lithium aluminium hydride (1.90g 20 m.moles) in dry tetrahydrofuran. The mixture was stirred at room temperature for 4 hours. A saturated solution of ammonium chloride (10 ml) was then added drop wise to destroy excess hydride and the reaction mixture was extracted with ether and worked up by method B, to yield 1.94g of residue. This residue was columned on silica and eluted with benzene/ethyl acetate mixtures, when the diol 14 (543 mg) was obtained pure, and 750 mg of enone-ester 8 were recovered. It did not prove possible to obtain this compound[14] in a sufficiently pure state for

micro-analysis, since even warming it on the steam bath was sufficient to induce oxidation, as evidenced by the appearance of a $\nu_{c=o}$ (liquid film) in the i.r. spectrum of warmed material. The following g.l.c. data was obtained :

Column	Temperature	Gas Flow Rate	Retention Time (mins)
5% QF1	175°	50 ml/min	4.0
5% QF1	150°	50 ml/min	8.2
5% QF1	125°	50 ml/min	22.6

The n.m.r. spectrum showed, at 4.35τ (1H) a broad multiplet ($W_{\frac{1}{2}}$ = 15Hz) due to the vinylic hydrogen, at 5.7τ (1H) a doublet (J = 3Hz) due to the hydrogen germinal to the secondary hydroxyl function and centred on 6.45τ (2H) a pattern typical of a conformationally frozen primary alcohol function arising above the broad base line peak for the OH protons. Interpretation of this pattern by the method of Bible [41] gives the following figures: δ_A 6.3τ, δ_B 6.5τ and J_{AB} = 10Hz. The solution i.r. shows ν_{OH} 3675 and 3635 cm^{-1}, due to free hydroxyl functions as well as a broad band extending from 3590 to 3100 cm^{-1} which decreases but does not disappear upon dilution. The vinyl hydrogen stretch frequency is 2990 cm^{-1} and the stretching frequency of the CH_2OH function can be seen at 2848 cm^{-1}. Other absorptions appear at 1445 (m), 1433 (m), 1412 (w), 1400 (w), 1069(s), 1045 (s), 1006 (s), 943 (w) and 686 (w) cm^{-1}.

1-(BICYCLO (5.3.1) UNDEC-7-ENE-11-ONYL)-METHANOL 15

Activated magnanese dioxide was prepared by the method of Attenburrow[46] and used as indicated below.

The diol(14) (51 mg) was dissolved in dry benzene (3 ml) and added drop wise to a stirring suspension of manganese dioxide (150 mg) in dry benzene (3 ml). The mixture was stirred at room temperature for 1 hour, when the oxidising agent was removed by filtration through celite, the filter pad being thoroughly washed out with hot benzene. The solvent was dried over anhydrous magnesium sulphate and then removed under reduced pressure to yield 50 mg of residue. Preparative t.l.c. gave 47.3 mg (93%) of 15. The g.l.c. data given below was obtained on a 4' column of 5% QF1 using a gas flow rate of 50 ml/min.

Column Temperature (^{o}C)	Retention Time (mins)
175	3.6
150	8.8
125	24.6

The molecular weight, as determined by mass spectroscopy was 194. The i.r. spectrum showed ν_{OH} at 3570 and 3640 cm^{-1} which did not change on dilution. Other bands appeared at 2970 (vinyl H stretch) 2865 cm^{-1} (C-H stretch of primary alcohol), 1683 (H-bonded carbonyl), 1458, 1385, 1053 and 1040. The n.m.r. spectrum showed, at 3.82τ (1H) a broad multiplet

($W_{\frac{1}{2}}$ = 8Hz) and, centred on 6.42τ (2H) the typical AB pattern[41] previously observed, with δ_A 6.17τ, δ_B 6.67τ and J_{AB}= 11Hz. The ultraviolet spectrum showed λmax 238 (ε = 4370).

PREPARATION OF A SUITABLE DERIVATIVE FOR X-RAY STRUCTURE ANALYSIS

PARACHLOROBENZOATE OF 15

p - Chlorobenzoyl chloride was prepared by the method of Wilds and Meader[47].

The primary alcohol 15 (54 mg 0.28 m.mole), pyridine (1 ml) and p- chlorobenzoyl chloride (0.5 ml) were refluxed together for 1 hour. A 5% aqueous solution of sodium bicarbonate (5 ml) was added and the ice cooled solution was filtered. The aqueous layer was extracted with ether and work up procedure B was used, to yield 17 mg of an oil. Storage of a solution of the product in 60 - 80 petrol at 0°C overnight gave a few micro-crystals, which were not suitable for X-Ray analysis. The compound obtained had the properties now described. The i.r. spectrum showed bands at 2855, 2925 cm^{-1}; 1725 cm^{-1} (aromatic ester); 1693 cm^{-1} (enone carbonyl); 1595, 1487, 1453, 1399, 1267, 1170, 1112, 1102, 1092, 1015, 847, 683 and 525 cm^{-1}. The n.m.r. spectrum showed at 2.0τ (2H), a doublet(J = 10Hz) due to the aromatic hydrogens ortho to the ester grouping, at 2.58τ (2H) a

doublet (J = 10 Hz) due to the aromatic hydrogens ortho to the chlorine atom, at 3.75τ (1H) a multiplet ($W_{\frac{1}{2}}$ = 10 Hz) due to the vinyl hydrogen and at 5.56τ (2H) a doublet J = 3 for the methylene group between C-1 and the aromatic residue. The mass spectrum showed a typical[48] benzoate ester cracking pattern. The parent ion could be seen at 332 (334 for ^{37}Cl) and the main fragments were at 306 and 304 (loss of C≡O from parent ion), 177 (loss of p Chlorobenzoate from P^{+}), 113 and 111 (the P-chlorobenzoate less CO_2), 141 and 139, 193, 176, 151 and 148.

PARABROMOBENZENE SULPHONATE OF 15

To the enone alcohol 15 (264 mg., 1.36 m.mole) in dry pyridine (1.6 ml) was added p-bromobenzene sulphonyl chloride (354 mg., 1.5 m.mole). The solution was allowed to stand at 0°C for 12 hours, when it was poured into 25 ml of 1N hydrochloric acid containing 5g of ice. The mixture was allowed to stand for 1 hour, after which it was extracted with ether. The ethereal extracts were washed with 1N hydrochloric acid and then work up procedure B was followed to give 373 mg, shown by t.l.c. to be 95% one compound, less polar than starting alcohol. A pure sample of this compound was obtained by preparative t.l.c. Attempts at crystallisation from 6 different solvent systems produced only an oil even at -70°. The i.r. (liquid film)

showed a transparent hydroxyl region, $\nu_{C=O}$ 1685, ν_{SO_2} 1180 as well as aromatic skeletal vibrations at 1580 and 1450 cm^{-1}, and the aromatic 1:4 disubstitution bands at 1070, 1010 and 840 cm^{-1}. Since the compound was not crystalline it was not characterised further.

p-CHLOROANILIDE OF 11-OXO, BICYCLO (5.3.1) UNDEC-7-ENE, CARBOXYLIC ACID (10)

11-OXO-BICYCLO (5.3.1) UNDEC-7-ENE CARBOXYLIC ACID CHLORIDE

The carboxylic acid (10) (1.91g, 9.2 m.mole) and redistilled thionyl chloride (6.5 ml 92.0 m.moles) were refluxed, with exclusion of moisture for 30 minutes. The volatiles were distilled off under reduced pressure and excess reagent removed by azeotroping with benzene, the product being distilled under reduced pressure. The acid chloride $b_{0.3}$ 140 - 145° was obtained in 68% yield.

The acid chloride (1.393g, 6.2 m.mole) was dissolved in dry benzene (5 ml) and treated with p-chloroaniline (0.805g., 6.3 m.mole) dissolved in dry benzene (5 ml), when a white precipitate formed immediately. The mixture was allowed to stand under nitrogen, with exclusion of moisture, at 0°C for 12 hours. The reaction mixture was poured into water (75 ml) and extracted with ether (3 x 25 ml). The

ethereal extracts were washed with 1$\bar{N}$ sulphuric acid (3 x 25 ml), saturated brine (1 x 10 ml.) saturated sodium carbonate (3 x 25 ml), 6$\bar{N}$ sodium hydroxide (1 x 15 ml) and saturated brine (2 x 10 ml) before drying over anhydrous magnesium sulphate. Solvent removal left 1.68g of residue which was columned on grade 1 (neutral) alumina (60g). Elution of the column with mixtures of 40/60 petrol through to 100% benzene gave the anilide in 74% yield from the acid chloride. Recrystallisation of the anilide from ethyl acetate was followed by drying at 50°C overnight, to give m.pt 87 - 8° (Found: C, 68.08; H, 6.39; N, 4.32. $C_{18}H_{20}NO_2Cl$ requires C, 68.02; H, 6.34; N, 4.41%). The i.r. spectrum (nujol mull) showed ν_{NH} 3430 $\nu_{C=O}$ 1690 cm^{-1} with aromatic absorptions at 1590, 1490 and 1400 cm^{-1} and amide bands at 1680 and 1530 cm^{-1}. A peak at 835 cm^{-1} confirmed the substitution pattern as 1:4. In solution the main absorption maxima were found at 3270, 1700, 1670, 1500, 1400, 1360, 1100 and 950 cm^{-1}. In the n.m.r. spectrum the typical $A'_2B'_2$ pattern[62] of a paradisubstituted aromatic ring was observed, centred on 2.6τ (4H). At 3.75τ (1H) a broad doublet (J = 2 Hz) due to the vinyl hydrogen and between 6.0 and 7.0τ (1H) a diffuse hump due to the amide hydrogen. The allylic hydrogens could be seen between 7.0 and 7.8τ (4H) and the methylene envelope between 7.8 and 9.2τ (10H). The u.v. spectrum showed λmax 250 ($\log \varepsilon = 4.35$).

The mass spectrum showed a parent ion at 317 (^{37}Cl at 319) and the main fragments were at 291,289, 191, 164, 163, 162, 136, 135, 134, 129, 127, 107, 93, 91, 81, 79, 77, 67 and 53. Crystals suitable for X-ray structure analysis were grown by slow evapouration of solvent from a saturated solution of the anilide in ethyl acetate (analar grade).

11 OXOBICYCLO (5.3.1) UNDEC-7-ENE CARBOXYLIC ACID (10)

The enone ester (8) (1.0gm.) was refluxed for 12 hours in 10% ethanolic sodium hydroxide solution (25 ml). The cooled reaction mixture was neutralised with 6N hydrochloric acid, flooded with water and thoroughly extracted with ether (10 x 15 ml). Work up procedure A was used to give 0.91g of residue, recrystallisation of which from 100 - 120 petrol gave 854 mg (92%) of a white crystalline solid m.pt 157 - 158°C. (Found: C, 68.97; H, 7.70 $C_{12}H_{22}O_3$ requires C, 69.21; H, 7.74%) The infra-red spectrum showed bands at 1759 cm^{-1} (carboxylic acid), 1700 cm^{-1} (unsaturated ketone), 3520 cm^{-1} (free hydroxyl) and a broad band from 3400 to 2500 cm^{-1} due to hydrogen bonded hydroxyl. The n.m.r. spectrum showed the low field signal (-1.1τ, 1H) characteristic of a carboxylate hydrogen, as well as at 3.7τ (1H), the broad multiplet ($\nu_{\frac{1}{2}}$7Hz) due to the vinyl hydrogen. The mass spectrum showed a parent ion peak of 208 with a strong peak at 164 ($P^{+} - CO_2$).

DECARBOXYLATION OF 11-OXO-BICYCLO (5.3.1) UNDEC-7-ENE CARBOXYLIC ACID (10)

The enone acid (21), (140 mg) was decarboxylated by the method[6] of Prelog, to yield 75 mg (68%) of product shown by t.l.c. and g.l.c. comparison with a known sample, to consist of the two enones (5) and (12) in the ratio 93:7.

ETHYL 7β, 8β DIBROMOBICYCLO (5.3.1) UNDECAN-11-ONE CARBOXYLATE (73)

The enone ester (8) (165 mg) was dissolved in carbontetrachloride and a solution of bromine in carbon tetrachloride was added drop wise with stirring until the brown colour was permanent. The solution was stirred for a further 10 minutes, when the organic layer was washed with aqueous sodium theosulphate, saturated brine and dried over anhydrous magnesium sulphate. Solvent removal left 256 mg of residue, out of which 34 mg of a product, mp 100 - 102°C was crystallised in a pure state from 60 -80 petrol. The mother liquor consisted of not less than 10 other compounds as seen by G.L.C. analysis. A solution i.r. of this compound showed $\nu_{c=o}$ 1720 (α Bromoketone) and 1735 cm^{-1} (ester). The n.m.r. spectrum showed a broad singlet ($W_{\frac{1}{2}}$ = 8Hz) at 5.30τ (1H) which could be assigned to a C - 8 equatorial hydrogen of the structure (73), as well as the signals

arising from the ester group 5.8τ (2H, q, J = 8 cps) and 8.7τ (3H), t, J= 8 cps).

METHYL 3-(2-OXOCYCLOOCTYL) PROPANOATE (74)

Alkylation of 1 - pyrrolidinocyclooctene was achieved by the method of Stork[43]. The keto ester (74) $b_{0.2}$ 94-5°, n_D^{25} 1.4732 (lit.[49] b_4 152°, n_D^{20} 1.4754) was obtained in 68% yield.

BICYCLO (5.3.1) UNDECAN-8, 11 - DIONE (21)

Ring closure of the keto-ester (74) was achieved by the method of Marshall and Scanio[14]. The dione (21) $b_{0.5}$ 108 - 110°, n_D^{17} 1.5132 (lit.[15] $b_{0.3}$ 97-8° n_D^{20} 1.5147) was obtained in 75% yield (See table 7 for $\nu_{c=o}$)

BICYCLO (5.3.1) UNDECAN-8, 11-DIOL (37)

Reduction of the diketone (21) to the diol (22) was achieved by the method of Marshall and Scanio[14]. The diol m.pt 114.5 - 115.5 (lit. 115 - 115.5°) was obtained in 68% yield.

BICYCLO (5.3.1) UNDECAN-8-OL-11-ONE TOLUENESULPHONATE (24)

This keto-tosylate was prepared by the method of Marshall and Scanio[14], except that the product was re-crystallised from ethanol, as fine white needles m.pt 118 - 118.5 (lit.[14] 118 - 118.5°). Yield 48%. The proton

of the tosylate-bearing carbon resonated as a seven line signal at δ 4.60 ($W_{\frac{1}{2}}$ = 17 Hz).

BASE TREATMENT OF KETO-TOSYLATE (24)

1. ETHANOLIC SODIUM ETHOXIDE

The keto-tosylate (24)(2.64g, 7.8 m.mole) was dissolved by warming in dry ethanol (50 ml). To the still-warm solution was added, with stirring, under nitrogen 8 ml of a 1.04 molar solution of sodium ethoxide (i.e 8.2 m.mole of NaOEt) in ethanol. After 5 minutes sodium p-toluene sulphonate was visibly precipitated. The solution was stirred for 14 hours at room temperature, when the t.l.c. showed no starting material remained. The reaction mixture was poured into 50 ml of ice-water and work up procedure A, using ether as solvent was used, to give 1.230 (96%) of a clear oil. The oil gave 1 spot on t.l.c. analysis but g.l.c. analysis revealed two peaks in the ratio 98:2. An analytical sample was obtained by distillation $b_{2.0}$ 83-4° n_D^{20} 1.5193 (Found: C, 80.5; H, 9.88, $C_{11}H_{16}O$ requires C, 80.44; H, 9.83%). The mass spectrum (see line diagram) showed the molecular ion at 164, with an intense peak at 136 (M-28) (see line diagram 1). G.L.C. analysis showed the compound to have a retention index of 1445 on 5% A.P.L. and of 1870 on 5% Q.F.1. The i.r. spectrum, run as a

liquid film showed a strong band at 3050 cm^{-1} (HC = C), $\nu_{C=O}$ at 1698 cm^{-1}, as well as sharp bands at 1381, 1155, 1122, 1098, 970, 962, 930, 800, 769 and 740 cm^{-1}. In CCl_4 solution the product showed i.r. absorption maxima at 3025 (w), 3000(w), 2925(s), 2850(s), 1702(s), 1699 (shoulder), 1684 (shoulder), 1450, 1440, 1430, 1375, 1150, 960, 950 and 918 cm^{-1}. When run as a solution in cyclohexane a band became clearly visible at 1696cm^{-1} with the $\nu_{C=O}$ at 1707 cm^{-1}. The n.m.r. spectrum showed, at 3.85τ (1H) a broad multiplet ($W_{\frac{1}{2}}$ = 9Hz) and the methylene envelope between 7 and 9τ (15H). This data is consistant with formulation of the product as bicyclo (5.3.1) undec-7-ene-11-one (5). A prolonged reaction time (40 hours) produced a product ratio of 80:20 of (5) to (12).

2. POTASSIUM HYDROXIDE IN AQUEOUS DIOXAN

A repeat of the method of Marshall and Scanio[14], using exactly the same conditions, quantities, reaction time and work-up procedure used by them, gave 103 mg of material which had composition similar to that obtained by method 1 above. However, by this method the ratio of the products was found by G.L.C. to be 98:2 before distillation. The

4.27τ 'multiplet' of Marshall and Scanio was little more than perturbation of the base line of the n.m.r. spectrum and integrated for less than 0.1H.

EQUILIBRATION OF ENONES (5) and (12)

A mixture of enones (5) and (12) in the ratio of 97:3 (7 mg) was heated at reflux for 60 hours in a mixture of glacial acetic acid (2 ml) and concentrated hydrochloric acid (0.5ml). Work up procedure B yielded the two enones (5) and (12) in the ratio 75:25 (7 mg) as determined by g.l.c. analysis.

BICYCLO (5.3.1) UNDEC-7-ENE-11-OL (55, R = H)

The enone (5) (150 mg; 0.92 m.mole) dissolved in anhydrous 1,2 dimethoxy ethane (2 ml) was added with stirring, under nitrogen, to a suspension of lithium aluminium hydride (60 mg; 1.5 m.mole) in 1,2 dimethoxy ethane (3 ml). G.L.C. analysis of worked up aliquots showed reaction to be complete after 30 minutes. Excess hydride was destroyed with a saturated aqueous solution of ammonium chloride. Work up procedure A using ether as a solvent yielded 155 mg of crystalline material. Recrystallisation of this material from 40 - 60 petrol gave material m.pt 91-92°, suitable for analysis (Found: C, 79.34; H, 10.79. $C_{11}H_{18}O$ requires C,79.46; H, 10.91%) The mass spectrum showed the molecular ion at m/e166 and

the main fragments at m/e 148, 109, 81, 79, 67 and 55 with the base peak at m/e 41. G.L.C. analysis showed the compound to have retention index of 1672 on a 5% Q.F.1. column (c.f enone (5) which has retention index 1870 on the same column). The infra-red spectrum showed ν_{OH} 36.30 cm^{-1} (secondary hydroxyl) ν vinylic hydrogen 3017 cm^{-1}, $\nu_{c=c}$ 1645 cm^{-1} (very weak) and other bands at 1455, 1446, 1076 and 1105 cm^{-1}. The hydroxyl absorption was sharp ($W_{\frac{1}{2}}$ 29 cm^{-1}) and showed no change on dilution. The n.m.r. spectrum showed at δ 5.38 (1H) a broad multiplet ($W_{\frac{1}{2}}$ 6Hz) due to the vinylic proton, at δ 4.44 (1H), the doublet of doublets typical of the M part of an AMX system[58]. The δ 4.44 signal collapsed to a doublet (J = 6Hz) upon irradiation of the δ 5.38 signal. This permits a more detailed interpretation of doublet of doublets observed for the carbinyl proton in the unirradiated spectrum, giving J_{AM} = 2.5 Hz, J_{MX} = 6 Hz and J_{AX} = ca 0 Hz and implying stereochemistry 55a for this compound (see discussion). The remainder of the n.m.r. spectrum consisted of a broad envelope between δ 3.0 and δ 1.0 (16H) due to the methylene protons.

BICYCLO (5.3.1) UNDEC-7-ENE-11-ONE (5)

To the allylic alcohol (55, R = H) (26 mg) in anhydrous benzene (3 ml) was added activated manganese dioxide[46]

(20 mg) and the solution was stirred at room temperature. After 1 hour a further 30 mg of oxidising agent was added and after 2 hours another 30 mg was added. The suspension was then stirred at room temperature for 60 hours, when g.l.c. analysis showed 100% conversion to pure αβ enone (5). The reaction mixture was filtered through celite and the solvent removed under reduced pressure. The enone (5) (18.9 mg., 73%) was obtained by preparative t.l.c. (15% ethylacetate in petrol). The ultra violet spectrum showed λ max 238 mm (ε 5,630).

EPOXIDATION OF ENONE (5)

1. ALKALINE PERHYDROL[27]

A solution of the enone (5) (30 mg), 8% aqueous sodium hydroxide (1 ml) 15% hydrogen peroxide (1 ml) and ethanol (1 ml) was warmed (steam bath) for two minutes and stirred at room temperature for 3 days, when it was flooded with ice water (10 ml). Application of work up procedure A using ether as solvent gave 22 mg of material shown (g.l.c.) to contain enone (5) (50%) and product 50%. The epoxide prepared in this way had R_I 2130 on 5% Q.F.1. and R_I 1545 on 5% A.P.L. when subjected to g.l.c. analysis.

2. PERACID

A solution of the enone (5) (55 mg., 0.34 m.mole), analar chloroform (2 ml) and m-chloroperbenzoic acid (60 mg., 0.4 m.mole) was stored at room temperature for 1 week. Analysis by t.l.c. and g.l.c. showed only product, having R_I 2130 on 5% Q.F.1. and R_I 1545 on 5% A.P.L. i.e. the same product as was obtained by method 1 above.

The epoxide obtained from 2 above was used in characterisation (Found: C, 73.09; H, 8.89. $C_{11}H_{16}O_2$ requires C, 73.30, H, 8.95%). The mass spectrum showed ions at m/e 180, 164, 152 and 137 as well as other, less abundant fragments. The n.m.r. spectrum showed at 6.68τ (1H) a singlet with some fine structure. The remaining protons appeared at between 7.4 and 8.9τ (15H). A solution infra-red spectrum showed maxima at 3090, 3070, 3038, 2970 (shoulder), 2910 —2960 (broad), 2885, 2858, $\nu_{C=O}$ 1732, 1724 (shoulder), 1468, 1457, 1446, 1440, 1361, 1344, 1328, 1275, 1126, 1115, 1038, 973, 920 (very intense) 896 (very intense) and 547 cm^{-1}.

The high carbonyl frequency is typical of a carbonyl with an α electronegative substituent[60].

ATTEMPTED MICHAEL ADDITION OF DIETHYL MALONATE TO ENONE (5)

This addition was attempted using the method of Bartlett et. al.[28]. Diethyl malonate (150 mg) was added, in anhydrous ethanol (2 ml) to a solution of sodium ethoxide in ethanol (0.02g sodium metal in 8 ml anhydrous ethanol) to give an ethanolic solution containing 0.90 m.moles of sodio-diethylmalonate. To this solution was added, over a period of 5 minutes, at 0°C, with stirring, the enone (5) (150 mg., 0.91 m.mole) in anhydrous ethanol (2 ml). When addition was complete the ice bath was removed and the solution stirred at room temperature for 48 hours. G.L.C. analysis of a worked up aliquot showed no adduct. The reaction mixture was then heated under reflux for a further 70 hours, cooled, poured into water and worked up by procedure A (ether) to yield 160 mg of clear oil. This was showsn (g.l.c.) to contain αβ enone (5) and βδ enone (12) in the ratio of ca 99:1, together with traces of diethyl malonate. There was no trace of an adduct when 0.5% would have been detected.

ATTEMPTED ADDITION OF 2, 4 DINITROBENZENE SULPHENYL CHLORIDE TO ENONE (5)

A mixture of enones (5) and (12) in the ratio 85:15 (164 mg., 1 m.mole), 2,4 dinitrobenzene sulphenyl chloride (235 mg., 1 m.mole) and glacial acetic acid (5 ml) was warmed (steam bath) for 15 minutes, stoppered and then

stirred at room temperature for 10 days. A starch/ potassium iodide test showed unreacted sulphenyl halide even after this period. The reaction mixture was poured into 10 g ice and work up procedure B using ethyl acetate as solvent gave 180 mg of yellow oil. This residue was applied to a preparative t.l.c. plate which was developed in 15% ethyl acetate in petrol.

Band A (Rf 0.6) yielded 60 mg of unreacted enones (5) and (12) in the ratio of 95:5, indicating faster consumption of βδ than of αβ enone by the sulphenyl halide reagent.

Band B (Rf 0.45) yielded 15 mg of material, showing the typical AMX pattern typical of the n.m.r. spectra of compounds containing the 2,4 dinitrosulphenyl function. The n.m.r. spectrum also showed the quartet (J = 7.5 Hz) of an ethyl group at 5.90τ (2H relative to aromatics) and a methylene envelope between 7.5 and 9.0τ (ca 11H), above which could be seen the triplet (J = 7.5 Hz) of the ethyl group. The i.r. spectrum showed bands at 1340 (Ar NO_2), 1600 (aromatic skeletal mode) and at 3105 and 3090 cm^{-1}. The highest mass number observed in the mass spectrum was at m/e 329.

Band C (Rf 0.3) yielded 41 mg of yellow amorphous material. The n.m.r. spectrum showed the same AMX system as was found in Band B. At 1.06τ (1H) a doublet (J_{AM} = 2Hz) due to the C-3 aromatic proton (H_A), at 1.64τ (1H) a doublet of

doublets (J_{AM} = 2Hz, J_{MX} = 8Hz), due to the C_5 aromatic proton (H_M) and at 2.31τ (1H) a doublet (J_{MX} = 8Hz) due to the C-6 aromatic proton. A multiplet ($W_{\frac{1}{2}}$ = 8.5 Hz) was observed at 5.90τ (2H) and the methylene envelope resonated between 7.0 and 9.0τ (16H). The i.r. spectrum of a saturated solution of this band in CCl_4 showed absorptions at 3090, 2960 and 2855 cm^{-1}, $\nu_{c=o}$ 1708 and 1595, 1525 and 1345 cm^{-1}. The spectrum was transparent below 1300 cm^{-1}. This data is consistant with addition of sulphenyl chloride to the βδ isomer (12).

OXIME OF ENONE (39)

A mixture of the enone (5) (70 mg), water (0.6 ml), hydroxylamine hydrochloride (150 mg), 10% aqueous sodium hydroxide (0.6 ml) and ethanol (1.0 ml) was refluxed for 6 hours and allowed to stand at room temperature for 12 hours. The reaction mixture was neutralised with 6$\bar{N}$ hydrochloric acid and work up procedure B, using ether as extractant gave 85 mg of a yellow oil which crystallised on standing. Recrystallisation of the product from nitromethane gave a white crystalline compound m.pt 117½ - 120°. Careful g.l.c. analysis of this crystalline substance showed 2 peaks in the ratio 50:50 (5% Q.F.1 at 115° - preheater at 180° - gas flow rate 50 ml/min), but each of the two compounds was obtained g.l.c. pure by preparative t.l.c., and since the two peaks had similar i.r.

spectra they were considered to be the syn and anti-isomers of 26. All characterisation was carried out on a mixture of the two isomeric oximes (26). (Found: C, 73.75; H, 9.42; N, 7.88. $C_{11}H_{17}NO$ requires C, 73.70; H, 9.56; N, 7.81%). The molecular ion appeared in the mass spectrum at m/e 179 and the main fragments at m/e 163, 147, 134, 119, 92 and 80. The solution i.r. showed maxima at 3600 (sharp) and a broad band from 3000 to 3100 as well as peaks at 2900, $\nu_{c=n}$ 1660, 1452, 1445, 1437, 1432, 1380, 1350, 1330, 1309, 1120, 1095, 1025, 987, 970, 958, 955, 948, 930, 912, 850 and 675 cm^{-1}. The n.m.r. spectrum showed, at 0.75τ (1H) a broad ($W_{\frac{1}{2}}$ = 21Hz) signal which disappears on addition of D_2O; at 4.3τ (1H) a multiplet ($W_{\frac{1}{2}}$ = 12 cps), at 6.41τ (0.5H) a broad ($W_{\frac{1}{2}}$ = 19 Hz) signal due to the bridgehead proton of the anti isomer between 6.84 and 7.17τ ($\frac{1}{2}$H) for the bridgehead proton of the syn form. The methylene envelope appeared between 7.2 and 9.2τ (14H).

ATTEMPTED REDUCTION OF OXIMES (26)

1. SODIUM BOROHYDRIDE IN ETHANOL

A mixture of the oximes (26) (22 mg 0.12 m.mole) in ethanol (3 ml) was added to a suspension of sodium borohydride (5 mg, 0.125 m.mole) in ethanol (2 ml). The solution was stirred at room temperature for 65 hours when the oximes were recovered, unchanged

(t.l.c./g.l.c./i.r.)

2. LITHIUM ALUMINIUM HYDRIDE IN TETRAHYDROFURAN

Treatment of the oximes (26) with L.A.H. in T.H.F. at room temperature for 24 hours resulted in quantitative recovery of starting material.

3. LITHIUM ALUMINIUM HYDRIDE IN REFLUXING 1.2 DIMETHOXY ETHANE

Overnight refluxing of the oximes as a D.M.E. solution in L.A.H. resulted in quantitative recovery of starting material.

BICYCLO (5.3.1) UNDEC-7-ENE-7-OL-11-ONE ACETATE (49)

The diketone (21) (360mg), isopropenyl acetate (10 ml) and paratoluene sulphonic acid (5 mg) were refluxed together for 114 hours. Most of the isopropenyl acetate was removed under reduced pressure and work up procedure A yielded 304 mg of residue, shown by t.l.c. and g.l.c. to contain ca 20% starting material. A sample of the product was obtained by preparative t.l.c. (Found C, 69.94; H, 8.18. $C_{13}H_{18}O_3$ requires C, 70.24; H, 8.16%). The molecular ion in the mass spectrum appeared at m/e 222. The i.r. spectrum showed $\nu_{c=o}$ 1758 (acetate) and 1704 cm^{-1} (11-one) and $\nu_{c=c}$

1675 cm^{-1}. Other bands appeared at 1455, 1430, 1200(s), 1190(s), 1138(s), 1088(s) and 1000 cm^{-1}. The compound had λ max 240 nm (ε 5,830). In the n.m.r. spectrum, between 7.35 and 7.7τ (5H) the allylic hydrogens and hydrogen α to carbonyl absorbed, at 7.81τ (3H) a sharp singlet appeared above the methylene envelope, and the methylene envelope resonated between 7.8 and 8.9τ (10H). This data is consistant with structure (49).

TREATMENT OF DIKETONE (21) WITH DIAZOMETHANE

To the diketone (21) (2.121g) in dry methanol (40 ml) was added an ethereal solution of diazomethane. The solution was allowed to stand in an ice bath and then at room temperature overnight. Total reaction time was 10 hours. G.L.C. analysis showed little starting material and two product peaks in the ratio 60:40. The larger of these (A) had a shorter retention time than starting diketone and the other (B) had longer retention time. The solvent was removed under reduced pressure after filtration through 'celite' to yield 2.136g of residue. Attempted separation of these two compounds by fractional distillation under reduced pressure yielded early fractions $b_{0.15}$ 78 - 80° which were enriched in compound A. Compound A was obtained in a pure state by preparative t.l.c. of these early fractions. Compound B was obtained by column chromatography,

of the higher boiling fractions ($b_{0.15}$ 80 - 84°), on basic alumina. Compound A was obtained as an oil ($b_{0.15}$ 79 - 80°, n_D^{20} = 1.5103) which showed $\nu_{c=o}$ (liquid film) 1720 and 1690 cm^{-1} in the i.r. spectrum and in the n.m.r. at 8.84τ (3H) a singlet. This data is consistant with that published[14] for 7-methylbicyclo (5.3.1) undecan-8, 11-dione (48).

Compound B was obtained as a white solid m.pt 73 - 73.5° (40 - 60 petrol) (Found: C, 74.00; H, 9.14. $C_{12}H_{18}O_2$ requires C, 74.19, H, 9.34%). It showed λmax 269 (ε = 8,660) in the u.v. The n.m.r. spectrum showed, at 6.26τ (3H) the singlet of the methoxyl, between 7.23 and 7.88τ (5H) an envelope due to the allylic and bridgehead protons and between 7.88 and 9.16τ (10H) the methylene envelope due to the ring protons. The i.r. spectrum showed ν_{C-H} 2930(s), 2842(w) and 2851(w) cm^{-1}, $\nu_{c=o}$ 1685 cm^{-1} $\nu_{c=c}$ 1643 cm^{-1} and other maxima at 1453, 1368(s), 1228(s), 1148(s) and 1105 cm^{-1}. The mass spectrum showed the parent ion and base peak at m/e 194 and fragments at m/e 179, 177, 166, 165, 162, 151, 140, 139, 137, 123, 111, 110, 109, 97, 93, 91 and 79. This data is consistant with formulation of B as 8 -methoxy bicyclo (5.3.1) undec-7-ene-one (47).

8,8-DIMETHOXYBICYCLO (5.3.1) UNDECAN-11-ONE (50)

A solution of the diketone (21) (10.8g, ca 60 m.mole), 2,2-dimethoxypropane (7.28g., ca 70 m.mole), methanol (50 ml) and p-toluenesulphonic acid (30 mg) was stirred at room temperature for 50 hours. The solution was neutralised with a methanolic solution of sodium methoxide and most of the solvent was removed under reduced pressure. Work up procedure B yielded 12.2g residue. Recrystallisation of the product from 40 - 60 petrol gave 10.2g (75%) of a crystalline product, m.pt 66-67°. (Found: C, 69.21; H, 9.94, $C_{13}H_{22}O_3$ requires C, 68.99; H, 9.80%) The molecular weight, as determined by mass spectroscopy was 226 with fragments at m/e 195, 194, 171, 135, 126, 109, 101, 97, 89, 88 and 79. The u.v. spectrum showed λmax 293 (ε = 20). In the n.m.r. spectrum signals at 6.83τ (6H), singlet (due to methoxyl protons), at 7.2 to 7.8τ (3H) and at 8.0 to 9.0 (13H) could be seen. The solution i.r. showed bands at 2960, 2930, 2865, 2848, 2830 cm^{-1}, $\nu_{C=O}$ 1703 and other maxima at 1442, 1350, 1272, 1235, 1105, 1062, 1055 and 1038 cm^{-1}. This data is consistant with the structure (50).

8-METHOXYBICYCLO (5.3.1) UNDEC-7-ENE-11-ONE (47) and 8-METHOXYBICYCLO (5.3.1) UNDEC-8-ENE-11-ONE (51)

1. BY DISTILLATION FROM SODIUM METHOXIDE OF KETAL (47)

A solution of sodium methoxide (prepared from 46 mg of sodium in 5 ml of rigorously dried methanol) was added to the ketal (50) (2.26g) in dry methanol (17 ml), in a distillation apparatus. The apparatus was heated in an oil bath until most of the methanol had distilled off at atmostpheric pressure, when the pressure was slowly reduced to 15 mm. This pressure was maintained and the flask heated to 100° for 1 hour. The product was then distilled out of the reaction mixture on oil pump vacuum; $b_{0.3}$ 96 - 102° when 1.684g (87%) of material was obtained. This was shown by g.l.c. to contain 3 compounds, in the ratio 90: 8 : 2. These 3 products were obtained in a pure state by column chromatography on basic alumina. The major product (90%) had all of the characteristics of the enol-ether (47), as reported earlier. The minor product (8%) was isolated but rapidly decomposed to diketone (21). The minor product (2%) had t.l.c., g.l.c. and i.r. identical to keto-ketal.

2. BY PYROLYSIS OF KETAL (47) IN TOLUENE

A solution of the ketal (47), (11.32g) and toluene-p-sulphonic acid (10 mg) in toluene (50 ml) was refluxed for 2 hours and then the solvent was distilled out, being replaced with fresh toluene until the distillate was 50 ml when distillation was stopped. The solution was refluxed for a further 2 hours and then the solvent was stripped off on the Buchi. The dry residue was taken up in ether, washed with 1N sodium hydroxide and saturated brine and dried over sodium sulphate. Solvent removal yielded 9.55g (98%) of t.l.c./g.l.c. pure material, consisting of the enol ethers (47) and (51) in the ratio 55:45 as determined by g.l.c. analysis.

ACTION OF PHENYL MAGNESIUM BROMIDE ON KETO-ENOL-ETHERS (47) and (51)

Phenyl magnesium bromide was prepared by the method of Allan and Converse[50].

To the enol ethers (47) and (51) (598 mg 3.1 m.mole) in anhydrous diethyl ether (10 ml) was added, portion wise, a solution of phenyl magnesium bromide in anhydrous ether (equivalent to 3.5 m.moles). The reaction mixture was allowed to stir at room temperature for 45 minutes, when it was poured into an ice-ammonium chloride-water bath. Extraction with ether, following work up procedure B, yielded 605 mg of yellowish crystalline material. This residue was subjected to column chromatography on silica, the main product being eluted with Benzene-Petrol (1:1). Combination of the relevant fractions gave 421 mg of white crystalline material. Re-crystallisation from 40-60 petrol gave m.pt 154-6°C. (Found : C, 79.23; H, 8.69

$C_{18}H_{24}O_2$ requires C, 79.37; H, 8.88%). The molecular weight as determined by mass spectroscopy was 272. Strong peaks appeared in the mass spectrum at m/e 254 (P-18) and at m/e 232 (P-40). The i.r. spectrum showed ν_{OH} 3600 cm^{-1} (sharp), ν_{Ar-H} 2855 and 2834, $\nu_{c=c}$ 1673 cm^{-1}, aromatics at 1490 and 1450 cm^{-1} and 3 sharp bands of medium intensity at 1208, 1168, 1052 cm^{-1} as well as the aromatic substitution band at 700 cm^{-1}. The n.m.r. spectrum showed two multiplets at 2.30 to 2.60 and 2.60 to 2.8τ (5H), for the aromatic protons, at 5.20τ (1H) a triplet (J = 4Hz) for the vinyl proton, at 6.40τ (3H) a singlet for the enol ether methyl function and at 7.0 to 7.3 a broad peak due to the OH proton. The methylene envelope resonated between 7.7 and 9.0τ (15H). This data is consistant with formulation of the product as 8-Methoxy, 11-phenyl bicyclo (5,3,1) under-8-ene-11-ol, with the stereochemistry at C-11 as indicated (53).

11-PHENYL BICYCLO (5.3.1) UNDEC-7(11)-ENE-8-ONE (52)

The hydroxy enol-ether (53) (63.4 mg) was dissolved in methanol (10 ml) containing paratoluene sulphonic acid (2 mg) and water (0.5 ml). The mixture was refluxed in an atmosphere of nitrogen, for 20 hours, when the solution was found to be bright green. Solvent removal, followed by work up procedure A, yielded 56 mg of yellow oil. The product was isolated by preparative t.l.c. when 40 mg of an oil (t.l.c., 1 spot; g.l.c., 1 peak) which was crystallised

from 40 - 60 petrol to m.pt 92 - 92.5°. (Found: C, 84.93; H, 8.45. $C_{17}H_{20}O$ requires C, 84.96; H, 8.39%). The molecular weight as determined by mass spectroscopy was 240. Strong fragment peaks appeared at m/e 239, 212 (M-28), 198 (M-42) and 183 (M-57). The g.l.c. analysis of this compound gave R_I 2704 on a 4' column of 5% Q.F.1. The ultra-violet showed λmax 308 (ε = 13,500). The n.m.r. spectrum showed, at 2.4 to 2.8τ (5H) a multiplet due to the aromatic protons, at 6.7 to 7.1τ (2H) a multiplet, at 7.1 to 7.5τ (3H) a multiplet, at 7.6 to 8.7τ (8H) a multiplet and at 8.7 to 9.4τ (2H) a multiplet. The i.r. spectrum (K Br disc) showed ν_{C-H} 2980, 2950, 2940, 2910, 2862 and 2850, $\nu_{C=O}$ 1640 (broad) and other maxima at 1604, 1595, 1590, 1565, 1488, 1451, 1445, 1440, 1420, 1359, 1299, 1200, 1145, 1077, 938, 762(s), 708, 693(s), 564 and 478 cm^{-1}. The hexane solution spectrum showed $\nu_{C=C}$ 1660 and $\nu_{C=C}$ 1652 cm^{-1}. The above data is consistant with formulation of the product as (52).

BICYCLO (5.3.1) UNDECAN-8-ONE-11-OL (54)

The keto enol ethers (6.5g., 33 m.moles of a 55:45 mixture of (47) and (51)) were dissolved in anhydrous ether (50 ml) and added drop wise to a stirring suspension of lithium aluminium hydride (1.27g., 33 m.moles) in anhydrous ether (50 ml). The reaction mixture was stirred at room

temperature for 19 hours. Excess hydride was destroyed with water (10 ml) and work up procedure B using ether as extractant gave 5.05g of residue. The residue was dissolved in dioxan (50 ml) and added to aqueous oxalic acid (20 ml of a 1M aqueous solution) and the solution stirred at room temperature for 23 hours. Work up procedure A yielded 4.85g of oily residue which gave 1 spot on t.l.c. analysis. 2.6g of this residue was chromatographed on 80g of silica, when 2.425g of t.l.c. and g.l.c. pure bicyclo-(5.3.1)-undecan-8-one-11α-ol (54) was obtained as a low melting volatile solid. (Found: C, 72.20; H, 9.96. $C_{11}H_{18}O_2$ requires C, 72.49; H, 9.95%). The molecular weight, as determined by mass spectroscopy was 182. Other significant peaks appeared at m/e 164 (M-18), 154 (weak), 140 (weak), 125 (strong, M-57). The u.v. showed λmax 282 (ε 38.5). The i.r. spectrum showed ν_{OH} 3625 cm^{-1}, ν_{CH} 2870 and 2925 cm^{-1}, $\nu_{c=o}$ 1713 cm^{-1}. Other absorption maxima were seen at 1469, 1454, 1442, 1333, 1310, 1221, 1074, 1065, 1018 and 1014 cm^{-1}. The n.m.r. spectrum showed, at 5.65τ (1H) a doublet of doublets, with some fine structure and at 7.0 to 8.9τ (17H), the methylene envelope. On addition of D_2O to the solution the doublet of doublets lost its fine structure and had $W_{\frac{1}{2}}$ = 14 Hz.

BICYCLO, (5.3.1) UNDECAN-8-ONE-11-OL METHANE SULPHONATE (59)

The ketol (54) (480 mg; 2.6 m.moles) was dissolved in anhydrous pyridine (4 ml) and added, with stirring, at 0°C under a nitrogen atmosphere to a solution of methane sulphonyl chloride (0.3 ml 3.9 m.moles) in anhydrous pyridine (2 ml). When addition was complete (15 minutes), the reaction mixture was stirred at room temperature for 4 hours. The reaction mixture was then poured into ice (15g) and extracted with benzene. The organic extracts were washed with 2M hydrochloric acid, saturated brine, 2M sodium carbonate, and again with saturated brine before drying over anhydrous magnesium sulphate. The drying agent was removed by filtration and the solvent removed under reduced pressure, using the minimum amount of heat, to yield 551 mg (80%) of an oil shown by t.l.c. in chloroform as solvent to be homogeneous (Rf 0.40) and different from starting material (Rf 0.13). The product was obtained as a microcrystalline white solid m.pt 60.5 to 61° (benzene /40-60 petrol). (Found: C, 55.16; H, 7.48. $C_{12}H_{20}O_4S$ requires C, 55.33; H, 7.74%) The molecular weight was 260 as determined by mass spectroscopy. Relatively intense peaks appeared at m/e 223, 203, 181, 165, 164, 149, 146, 136, 135, 124, 123, 122, 121, 109, 108, 107, 95, 93 and 69. The n.m.r. spectrum showed at δ 5.17 (1H) an assymetric quartet ($W_{\frac{1}{2}}$ = 14Hz)

(M of AMX with J_{AM} = 2Hz and J_{MX} = 5Hz), at δ 3.o (3H), singlet (methyl of sulphonate ester) and between δ 2.8 and δ 1.0 (16H) the methylene envelope. The i.r. spectrum showed bands at 2925, 2865, $\nu_{C=C}$ 1715, 1367, 1346, 1328, 1178(s), 946, 893 and 522.

BICYCLO (5.3.1) UNDEC-7(11)-ENE-8-ONE (4)

1. N.N DIMETHYL FORMAMIDE

The keto mesylate (59) (43.7 mg) was dissolved in anhydrous N,N dimethyl formamide (2 ml) and refluxed under nitrogen for 90 minutes. Most of the solvent was removed under reduced pressure and the residual material was applied to a preparative t.l.c. plate made up using HF 254 silica, the plate being developed with 30% ethyl acetate in petrol. Irradiation of the developed plate with u.v. light (254 nm) showed a band of Rf 0.5 which, when extracted with ether yielded 25 mg of pale yellow oil, which showed one peak on g.l.c. analysis (R_I 1888 on 5% QF1) and one spot on t.l.c. analysis (Rf 0.57 in 25% ethylacetate/petrol). The compound showed λ_{max}^{EtoH} 255 and had a molecular ion in the mass spectrum at m/e 164. The i.r. spectrum showed $\nu_{c=o}^{CCl_4}$ 1675 cm^{-1}.

2. 1,5 DIAZABICYCLO (4,3,0) NON-5-ENE (D.B.N.)

To the oxomesylate (59) (3.86g, 14.9 m.mole) in benzene (70 ml) was added, drop wise, with stirring, under nitrogen D.B.N. (4.1g, 33 m.mole) in benzene (80 ml). After 15 minutes a white solid began to be precipitated and when addition was complete (30 minutes) the reaction mixture was stirred for a further hour. The solution was filtered to remove $D.B.N.H^+ MeSO_3^-$ and solvent removed on the Buchi. Addition of ether to the dry oily product caused precipitation of more salt, which was filtered off. The filtrate was washed with saturated brine (2 x 50 ml), 1N HCl (4 x 50 ml) and saturated brine (2 x 25 ml), dried over sodium sulphate and the ether removed to give 1.80g of yellow oil. Distillation gave 1.26g of colourless oil, (n_D^{25} 1.5356), identical with the compound obtained by method 1 above. (Found: C, 80.62; H, 9.62. $C_{11}H_{16}O$ requires C, 80.44; H, 9.82%) Line diagram 2 is a representation of the mass spectrum of this compound. The compound showed λ_{max}^{EtoH} 255 (ε 7,500). The i.r. spectrum showed peaks at 2925, 2865, $\nu_{c=o}$ 1675, $\nu_{c=c}$ 1622, 1449, 1427, 1382, 1178, 1158, 1092, 975, 947, 898 and 891 cm^{-1}. The spectrum, when run in hexane showed $\nu_{c=o}$ 1678

and $\nu_{c=c}$ 1622 cm^{-1}. The n.m.r. spectrum showed, at δ6.85 (1H) a doublet (J = 4.5 Hz), at δ 2.95 (2H), a multiplet ($W_{\frac{1}{2}}$ 13 Hz), at δ2.7 - 2.3 (2H) a multiplet, at δ 2.3 to 1.1 (9H), the methylene envelope and at δ1.1 to 0.3 (2H) a broad absorption.

2 METHYL CYCLOHEX2ENE 1ONE

This model compound was prepared by the method of Warnhoff et.al.[59]. The vinyl proton signal in the n.m.r. appeared at δ6.66(1H) as a broad multiplet ($W_{\frac{1}{2}}$ = 8 Hz).

2 METHYL CYCLOHEX 2 ENE-1-OL

A solution of 2 methyl 2 cyclohexenone (1g., 9.1 m.mole) in anhydrous ether (10 ml) was added drop wise, with stirring to a suspension of lithium aluminium hydride (150 mg., 4.2 m.mole) in anhydrous ether (10 ml). The reaction mixture was stirred at room temperature overnight. Excess hydride was destroyed with a saturated aqueous solution of ammonium chloride. Work up procedure A yielded 930 mg of product containing ca 5% (g.l.c.) of starting material. A sample of the pure alcohol was obtained by preparative t.l.c. using 10% ethyl acetate in petrol as solvent system. The product showed ν_{OH}^{film} 3430 cm^{-1} and other bands at 1450, 1060, 990, 960 and 815 cm^{-1}.

The n.m.r. spectrum showed, at δ 5.56 (1H) a broad multiplet ($W_{\frac{1}{2}}$ = 8 Hz) due to the vinyl proton, at δ4.00 (1H) a broad multiplet ($W_{\frac{1}{2}}$ = 7.5 Hz) due to the carbinyl proton, and at δ2.2 - 0.9 (10H) the remainder of the protons. The methyl singlet appeared at δ1.70.

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